STUDY OF PSYCHIATRIC MANIFESTATIONS AND QUALITY OF LIFE AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

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CERTIFICATE

This is to certify that the dissertation titled, **"STUDY OF PSYCHIATRIC MANIFESTATIONS AND QUALITY OF LIFE AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS"** is the bonafide work of **Dr. ARCHANA G**, in part fulfillment of the requirements for M.D. Branch – XVIII (Psychiatry) examination of The Tamilnadu Dr. M. G. R. Medical University, to be held in April 2013. The period of study was from May 2012 – OCTOBER 2012.

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DECLARATION

I, **Dr. ARCHANA G**, solemnly declare that the dissertation titled, **"STUDY OF PSYCHIATRIC MANIFESTATIONS AND QUALITY OF LIFE AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS",** is a bonafide work done by me at the Madras Medical College, Chennai, during the period from May 2012 - October 2012 under the guidance and supervision **of Dr. JAYAPRAKASH. M.D, D.P.M,** Professor of Psychiatry, Madras Medical College.

The dissertation is submitted to The Tamilnadu Dr. M. G. R. Medical University towards part fulfillment for M.D. Branch XVIII (Psychiatry) examination.

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1. INTRODUCTION

The ‘lupus’ term has its root in Latin language which means ‘wolf’ and was used for the first time to describe skin lesions which are erosive and it resembles a ‘wolf’s bite’. Ferdinand von Hebra, a physician from Viennese introduced the metaphor ‘butterfly’ to portray ‘malar rash’ in 1846. He used the term ‘lupus erythematosus’ to illustrate in his book ‘Atlas of Skin Diseases’ in 1856. Moriz Kaposi was the first one to recognize lupus as a systemic disease with visceral manifestations. After the discovery of ‘LE’ cell by Hargraves, Morton and Richmond in 1948 at Mayo Clinic the modern age began in SLE. In late 1950’s it was discovered that lupus patients had high levels of circulating autoantibodies against nuclear structures (anti-nuclear autoantibodies; ANA) and diagnostic immunofluorescence assays were developed for the demonstration of ANAs.

It is now recognized that systemic lupus erythematosus (SLE) is a chronic autoimmune disease with involvement of multiple systems. This disease presents with a variety of clinical manifestations and the course of the disease is highly variable with several exacerbations and remissions. During the course of the disease, a range of psychiatric manifestations have been reported. It is said that the prevalence of psychiatric morbidity, notably anxiety and mood disorders is common. The reported prevalence rates range from 17% to 75% (Shehata et al, 2011). Apart from

psychiatric manifestations, neurological disorders like stroke, seizure and headache have also been reported. The prevalence of neuropsychiatric manifestations has influenced the classificatory system in recognizing two types of SLE namely, neuropsychiatric SLE (NPSLE) and non-NPSLE patients. Cognitive impairment is important parameter in NPSLE.

Despite its importance and relevance, studies in India related to assessment of psychiatric manifestations are scanty and the present study is an attempt at assessment of psychiatric manifestations in patients with SLE.

2. REVIEW OF LITERATURE

DEFINITION AND CLASSIFICATION

"Systemic lupus erythematosus (SLE) is a chronic relapsing remitting autoimmune disorder mediated by the immune-complex and characterized by its protean clinical manifestation and multisystem involvement". The disease occurs commonly in young women and the severity varies from mild symptoms like a simple rash to more complex problems like arthritis and disease is characterized by involvement of renal and nervous system (Pisetsky 1997). The classification of SLE is by 11 criteria suggested by the American College of Rheumatology (ACR) and later revised (Hochberg 1997, Tan et al 1982).

AMERICAN RHEUMATISM ASSOCIATION (ARA) 1997 REVISED CRITERIA FOR THE CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

"1. Malar rash → Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds.

2. Discoid rash → Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions.

3. Photosensitivity → Skin rash as a result of unusual reaction to sunlight, by patients' history or physician observation.

4. Oral ulcers → Oral or nasopharyngeal ulceration, usually painless, observed by a Physician

5. Arthritis → Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion

6. Serositis → a) Pleuritis – convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion

OR

b) Pericarditis

7. Renal disorder → a) Persistent proteinuria greater than 0.5 per day or greater than 3+ if quantification not performed

OR

b) Cellular casts

8. Neurologic disorder → a) Seizures – in the absence of offending drugs or known metabolic derangements: e.g.,uremia, ketoacidosis, or electrolyte imbalance

OR

b) Psychosis – in the absence of offending drugs or known metabolic derangements: e.g., uremia, ketoacidosis, or electrolyte imbalance

9. Hematologic disorder → a) Hemolytic anemia

OR

b) Leukopenia – less than 4000/mm total on two or more occasions

OR

c) Lymphopenia – less than 1500/mm on two or more occasions

OR

d) Thrombocytopenia – less than 100000/mm in the absence of offending drugs

10. Immunologic disorder → a) Anti-DNA: antibody to native DNA in abnormal titer

OR

b) Anti-Sm: presence of antibody to Sm nuclear antigen

OR

c) Positive finding of antiphopsholipid antibodies

11. Antinuclear antibody → An abnormal titer of antinuclear antibody at any time and in the absence of drugs known to be associated with drug-induced lupus syndrome."

The classification is based on 11 criteria. SLE can be diagnosed when 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.

EPIDEMIOLOGY

SLE is a worldwide disease; incidence peaks from 15 to 40 years of age with an average age of 32 years for disease onset in women while 40 years of age for men (Pisetsky 1997). Multiple organs are affected in women 9 times more commonly than men (Muscal et al 2010). 90% of women are in child bearing age; people of both sex, all ages, and all ethnic groups are susceptible. Incidence and prevalence rates vary in the world depending on genetic and environmental factors. The incidence is 2.4 % per 100,000 across genders and race, 9.2 % per 100,000 for black woman and 3.5 per 100,000 for white woman. It is more common in African-Americans, African-Caribbeans and Asians, than in Caucasians.

CLINICAL MANIFESTIONS

General features of SLE include fatigue, malaise, fever and weight loss (Pisetsky 1997). Fatigue occurs in almost all patients. Low-grade fever is common; it may reflect active disease or infection. Weight loss occurs in about 60% of patients (Schur 1996).

Arthritis and/or arthralgia affect 85 - 90% of patients during the course of illness. Arthritis predominantly affects the small joints of the wrists, hands and knees and can be deforming, although it does not produce joint erosion (Pisetsky 1997)

The skin is involved in most SLE patients. A wide variety of skin manifestations include butterfly rash, discoid rash, photosensitivity,

livedo reticularis, mucous membrane lesions, alopecia and vasculitic skin lesions (Schur 1996).

Pericarditis occurs in about 25% of patients (Rothfield 1996). Asymptomatic valvular lesions are detected by ECHO in 25% of patients but Libman-Sacks endocarditis is rarely seen. Occasionally it can be associated with antiphospholipid syndrome (APS) (Pettersson et al 2005). Lung is involved in about 50% of SLE patients with pleuritis being most common (Schur 1996)

Renal disease is a frequent manifestation and develops in about 50%-75% of patients (Schur 1996; Pisetsky 1997). Only few patients develop clinical renal disease, but most patients have some histologic abnormalities of the kidneys. The basic lesion is glomerulonephritis (GN). Renal biopsy is important in assessment of the nephritis pattern and the reversibility of the lesion.

The 1982 World Health Organization grading system is currently used

TYPE1 : Normal kidney

TYPE 2: Mesangial Glomerulonephritis

TYPE 3: Focal segmental proliferative glomerulonephritis

TYPE 4: Diffuse proliferative glomerulonephritis

TYPE 5: Membranous glomerulonephritis

TYPE 6: Chronic sclerosing glomerulonephritis

The higher the grade, more severe is the renal involvement (Burnett et al 2005).

Muscle pain is a frequent complaint and accompanied occasionally by muscle wasting and weakness. True myositis is uncommon (Schur 1996).

One or more hematological abnormalities are present in nearly all patients with active disease (Rothfield 1996). They may reflect nonspecific inflammatory effects on bone marrow activity as well as binding of antibodies to elements of blood cell. Generalized lymphadenopathy is very common especially with active disease. Anti-phospholipid antibodies (APL) can be found in 20-35% of patients with SLE (Pisetsky 1997).

It may involve any ocular structure. The most common ocular manifestation is xerostomia (Rosenbaum et al 1996).

Gastrointestinal symptoms are common, complaints include nausea, vomiting, dyspepsia and abdominal pain. Etiologies include bowel vasculitis, diffuse peritonitis, pancreatitis, inflammatory bowel disease or the use of medications (Schur 1996).

Neuropsychiatric (NP) manifestations will be discussed later.

The typical course is of flares and remissions, sometimes with many months or years between periods of clinical activity. The disease activity measures include monitoring laboratory tests and clinical

symptoms. The valid indices available to measure disease activity and damage index are:

“SLAM - Systemic Lupus Activity Measure

SLEDAI - Systemic Lupus Erythematosus Disease Activity Index

LAI - Lupus Activity Index

BILAG - British Isles Lupus Activity Group

ECLAM - European Consensus Lupus Activity Measure.”

The survival rate of SLE patients has increased when compared to the past forty years from 5 year survival of <50% by 1955 to survival rate of > 90% in recent studies. Leading cause of fatality in SLE patients is infection which may be owing to complication of either active disease or its treatment. Other major causes of death are pulmonary, renal or CNS failure and premature coronary artery disease (Boumpas et al 1995; Schur 1996; Doria et al 2006). In a recent study SLE patients had a mortality rate four times higher when compared to common people and malignancy being the most common reason; it is followed by infection and vascular disease. Deaths in younger age were as a result of renal disease and late deaths were owing to atherosclerosis (Moss et al 2010).

PATHOGENESIS

The etiology of SLE is not known. As with most autoimmune diseases, multiple factors likely effect it.

Genetic susceptibility

A strong familial aggregation is present in SLE and high frequency of first degree relatives being affected than others. In identical twins, the concordance rate is nearly 25-50% while in dizygotic twins is around 5%. These findings lead us to the fact that genetic factors are one of the important contributing factors for the causality of SLE. In most cases, multiple genes interact with one another to cause the disease but rarely single gene could lead on SLE. Linkage analyses have been used in increasing frequency now a day to find the susceptibility genes. An estimate says that for the disease to occur, at least four susceptibility genes should be inherited. Human leucocyte antigen (HLA) class II gene polymorphisms are implicated in susceptibility to SLE in general population. HLA DR2 and DR3 allele and SLE association is commonly present in patients belonging to various ethnicities and this association increases the risk of by fivefold for them to develop the disease. However, in general population, SLE cases are sporadic and with no genetic predisposing factors. This finding suggests that many environmental or yet unknown factors may also be contributing for the

causality of the disease (Mok & Lau 2001; Sawalha & Harley 2004; Tsao 2004).

Role of hormones

Endogenous sex hormones have a role in predisposing the individual to the disease. SLE is a disease which is commonly seen in female gender and it usually flares up before puberty or after menopause. Oestrogen metabolism is disturbed in both male and female patients and plasma androgen levels are low in women who are having SLE. Usually, SLE flares up when the hormone levels are altered quickly. Further evidence suggests that activity as well as prognosis of SLE depends on the concentration of endogenous oestrogen. Prolactin, an immunostimulatory hormone, levels are raised in SLE. Hormones create an internal milieu which makes the person susceptible for the development of the disease (Mok & Lau 2001).

Environmental triggers

Genetic and the hormonal factors lead only to susceptibility for the development of the disease but the initiation is by environmental triggers and some factors which are exogenous. Environmental triggers suggested in the initiation of SLE are chemical and physical factors like drugs (procainamide, isoniazid, hydralazine, quinidine, methyl DOPA and chlorpromazine), hair dyes, tobacco smoke, aromatic amines, hydrazines and UV light. Some dietary factors like high intake of saturated fats have

been suspected to precipitate SLE. Theoretically, infectious agents such as viruses might flare up SLE by molecular mimicry. Viruses suspected to be involved in pathogenesis of SLE are Epstein-Barr virus, cytomegalovirus, parvovirus B19 and the retroviruses. Hormones and environmental oestrogens have been linked to autoimmune disorders. Hormonal replacement therapy and oral contraceptive pills are related to a mild risk of SLE initiation (Mongey et al 1996; Mok & Lau 2001, Manson & Isenberg 2003).

Immunopathology

Multiple immunologic pathologies are implicated for the initiation and clinical picture of SLE (Anolik & Sanz 2004). The basic pathological features are chronic inflammation and abnormalities in blood vessels (Mok & Lau 2001). The fundamental disturbance appears to be a dysfunction of immune system, with a loss of self-tolerance caused by alterations in B-cell functions. The disease is characterized by autoantibody production and immune-complex-mediated end-organ damage; both of them reflect the failure of immune tolerance (Burnett et al 2005; Tieng et al 2007).

The central immunological disturbance is autoantibody production by B cells. There is evidence that depending on genetic background and specific environmental insults, the disease may be induced by a

breakdown of B-cell tolerance leading to the generation of pathogenic antibodies (Anolik & Sanz 2004). Autoantibodies for the nucleus, cytoplasm, and cell surface are usually found. In addition various autoantibodies may be used to diagnose, predict the disease manifestations and be helpful in monitoring the disease activity and response to treatment (Sawalha & Harley 2004).

Antinuclear antibodies (ANA) are distinct and sensitive since it is present in more than 95% of the people suffering from SLE (Manson & Isenberg 2003; Mok & Lau 2001;Sawalha & Harley 2004). But ANA are not specific as it is present in other autoimmune, rheumatic, and infectious conditions and even in normal individuals. Diagnosis of SLE does not solely rest on the presence of ANA. Recent demonstration that patients with SLE may express ANA many decades or years before clinical disease sets in suggesting B-cell tolerance is an important factor in the pathogenesis of SLE and it is broken down early in the disease. This B-cell breakdown can lead to other immune malfunctions (Anolik & Sanz 2004; Sawalha & Harley 2004; Doria et al 2008). The antibodies with the highest specificity for the diagnosis of SLE are those directed toward dsDNA (Anti-dsDNA) (Mok & Lau 2001; Manson & Isenberg 2003). Anti-dsDNA is not particularly sensitive because it may only be transiently detected in the course of disease. Other autoantibody which is unique in SLE is Anti-Sm antibodies (Sawalha et al 2004, Mok et al

2005). The other important antibody in SLE is anti-dsDNA antibodies and it is associated with glomerulonephritis. Raised anti-dsDNA antibody titers have been found in active lupus nephritis. Anti-dsDNA antibodies are deposited in various parts of the body but it has a selective deposition in the kidneys and this antibody deposition leads to inflammation. Anti-dsDNA antibody titers vary with time but not so in the case of anti Sm antibody titres. In addition to the above said antibodies, a host of other autoantibodies are present in SLE. The antigens against which the antibodies are produced depends on patient ethnicity or particular disease manifestations (Manson & Isenberg 2003)

T cell functions are also aberrant in SLE patients. The number of activated T cells has been found to be increased in peripheral blood in SLE patients. The activated T cells act upon the B cells and induce it to produce autoantibodies (Mok & Lau 2001; Hoffman 2004; Kyttaris et al 2004). T-cells, which suppress the self-directed B-cells, also malfunction in SLE (Manson & Isenberg 2003).

Cytokines are proteins, low in molecular weight and act as immune system modulators. T-helper cells secrete Interleukin-10 (IL-10) which stimulates the B-cell for its proliferation and antibody production. The serum concentrations of IL-10 are significantly higher in SLE patients. Research findings show us that IL-10 is responsible for the overproduction of antibodies observed in SLE (Mok & Lau 2001;

Manson & Isenberg 2003). Tumour necrosis factor α (TNFα) gives some protection from SLE (Manson & Isenberg 2003).

During the flare ups of SLE, there is a diffuse vasculopathy in endothelium. Adhesion molecules also mediate some cellular interactions which lead on to inflammatory process. Up regulation of Vascular cell adhesion molecule-1 (VCAMI) is seen in SLE (Merrill et al 2005).

COMMON ANTINUCLEAR ANTIBODIES IN SLE (Sawalha & Harley 2004).

Autoantibody	**Frequency (%)**	**Autoantigen**
Anti-dsDNA	50-60	DNA double helix
Anti-Sm	10-25	Spliceosomal snRNP
Anti-Ro (SS-A)	25-40	60-kDa or 52-kDa proteins
Anti-La (SS-B)	10-15	48-kDa proteins
Anti-Ribosomal P	15	Ribosomal phosphoproteins P0, P1, P2
Anti-nRNP	23-40	Spliceosomal snRNP
Anti-Histone	50-70	H1, H2A, H2B, H3, H4, H5
Anti-Ku	20-40	p70/80 proteins

dsDNA, double-stranded DNA; Sm, Smith; snRNP, small nuclear ribonucleoprotein; nRNP, nuclear ribonucleoprotein.

Apoptosis

Evidence implicates apoptosis, programmed cell death, is a way by which propagation of SLE may happen and it is precipitated by various factors. This results in elevation in antibody production. Recent literature shows that there is a defect in apoptotic cell clearance function in SLE. The reason could be the deficiency of early complement proteins, such as C2, C4, or C1q and patients with these deficiencies may develop into severe lupus-like disease early in life (Mok & Lau 2001; Manson & Isenberg 2003). There is a high concentration of microparticles, which are small membrane-bound vesicles that reduces phagocytosis of apoptotic cells. In SLE, there have been measured raised levels of microparticles (Antwi-Baffour et al 2010).

Definition and classification of neuropsychiatric SLE (NPSLE)

"Neurologic and psychiatric manifestations have been termed ***CNS vasculitis, CNS lupus, neurolupus, neuropsychiatric lupus,*** **or** ***lupus cerebritis"***. It includes neurologic syndromes of central, peripheral, and autonomic nervous system. It is estimated that two thirds of NP manifestations in SLE are not directly related to active NPSLE (primary NPSLE) but instead are a consequence of SLE like infections, drugs and hypertensive and metabolic complications (secondary NPSLE). The NP symptoms vary in their clinical expression from focal to diffuse

manifestations (Kovacs et al 1993). They can also be divided to major symptoms, including e.g. Cerebrovascular events, seizures and psychosis; and minor symptoms e.g. headaches, mood swings and cognitive complaints (Denburg et al 1993). As there is no one test available sensitive and specific enough to diagnose NPSLE, the diagnosis and management of each patient is based on clinical and other investigations and tests (Brey 2007). NPSLE syndromes can occur at any time of the disease course and even when there is no disease activity is present outside the nervous system. In approximately 28% - 40% of the patients predisposed to develop SLE, NPSLE symptoms occur before the start of SLE, or while diagnosis and in 63% of persons NPSLE symptoms can be seen after one year of diagnosis (Brey 2007; Burnett et al 2005). NPSLE has been reported to be a prognostic factor for a poor long-term outcome in SLE. In a recent study, the occurrence of NP events in newly diagnosed patients, a relationship was seen between reduction in quality of life scores and increased organ damage (Hanly et al 2007). The mortality rate in NPSLE has varied from 7% to 40% and NP involvement constitutes the second prevalent reason for death in SLE after renal failure (Kovacs et al 1993; Sibbitt et al 1999).

The Neuropsychiatric Syndromes In SLE According To The American College Of Rheumatology Nomenclature And Case Definitions (ACR Ad Hoc Committee On Neuropsychiatric Lupus Nomenclature 1999).

Central Nervous System

Aseptic meningitis

Cerebrovascular disease

Demyelinating syndrome

Headache

Movement disorder (chorea)

Myelopathy

Seizure disorders

Acute confusional state

Anxiety disorder

Cognitive dysfunction

Mood disorder

Psychosis

Peripheral nervous system

Acute inflammatory demyelinating Polyradiculoneuropathy

Autonomic disorder Mononeuropathy, single/multiplex

Myasthenia gravis

Neuropathy, cranial Plexopathy

Polyneuropathy

Clinical features of NPSLE

Central nervous system

Aseptic meningitis

Aseptic meningitis is a non-infectious meningeal syndrome which may present with some nuchal rigidity and increased cells in cerebrospinal fluid. Aseptic meningitis is not a very presentation, but it can occur in early phase of disease. It has multiple factors for initiation. The immune complex deposition in the choroid plexus has been suspected in pathogenesis. When making a diagnosis of aseptic meningitis as a part of active SLE, nonsteroidal anti-inflammatory drugs (NSAID) as a potential cause must be excluded. Aseptic meningitis as a side effect of NSAID is probably more common in SLE patients than in others (Kovacs et al 1993; Ostensen & Villiger 2001; Jennekens & Kater 2002).

According to the ACR case definitions, “A diagnosis of aseptic meningitis can be made when we observe symptoms and signs such as acute or subacute onset of headache, photophobia, neck stiffness and fever, signs of meningeal irritation and abnormal CSF (ACR 1999)”.

Cerebrovascular

Stroke occurs in patients with SLE by a variety of mechanisms, including cardiogenic embolus, large-vessel occlusion or stenosis, small-vessel ischemia, and intracranial hemorrhage. In SLE, ischaemic stroke is correlated to the presence of circulating antiphospholipid antibodies and premature atherosclerosis (Jennekens & Kater 2002). The estimated frequency of strokes and transient ischemic attacks (TIA) among SLE patients ranges from 3% to 19 %. Futrell and Millikan reviewed 105 patients with SLE and found that the majority of patients had their first cerebrovascular accident within the first 5 years of illness and the mean age of patients at the time of stroke was 40 years (Futrell & Millikan 1989). SLE patients have a high risk for recurrent cerebral ischemia and the risk may be over 50% (Kovacs et al 1993).

The ACR case definitions suggest the following diagnostic criteria for cerebrovascular disease: “stroke syndrome, TIA, chronic multifocal disease, subarachnoid and intracranial hemorrhage and sinus thrombosis; supporting radioimaging study must be included and antiphospholipid antibodies (APL) recorded (ACR 1999)”. In newer studies using ACR case definitions the prevalence of cerebrovascular disease has varied from 2% to 24% (Brey et al 2002; Sanna et al 2002; Afeltra et al 2003; Hanly et al 2004)

Demyelinating syndrome

The phrase “lupoid sclerosis” represents patients with SLE having complex neurologic deficits. It refers to relapsing myelopathy or optic neuropathy (ACR 1999; Jennekens & Kater 2002; Hanly et al 2005). In CSF, oligoclonal bands may be seen and multifocal white matter bright spots may be seen on magnetic resonance imaging (MRI) studies.

ACR case definitions recommend the term “demyelinating syndrome” to be used instead of “lupoid sclerosis” (ACR 1999).

Headache

Headache is a common symptom both in SLE patients and in the normal population; whether there is a unique syndrome attributable to SLE is debated (Liang & Karlson 1984; ACR 1999, Hanly et al 2005). Studies have reported the prevalence ranging from 30% to 65% (Mitsikostas et al 2004). Isenberg et al reported the first controlled trial that concludes migraine with aura was more common in SLE than control population (Isenberg et al 1982). The incidence of migraine was prospectively studied in 90 patients and controls; a history of migraine in SLE patient group (34%) was approximately twice as common as in controls. An association between migraine and SLE disease activity was found too (Markus & Hopkinson 1992). In two recent controlled studies

the prevalence of headache in SLE has been investigated. In the first one, migraine was notably more common among patients with SLE when compared with patients with rheumatoid arthritis (RA), and related with SLE activity and organ damage measured by SLICC (Appenzeller & Costallat 2004). In another study, headaches were also more widespread in SLE patients than in RA patients. The scores for SLE disease activity or damage, functional disability and quality of life were similar between patients who suffered from SLE headache compared to those without SLE headache (Weder-Cisneros et al 2004). Both studies agreed that Raynaud`s phenomenon is related either with migraine or headache in general in patients with SLE.

ACR case definitions includes “migraine without aura, migraine with aura, cluster headache, tension headache, headache from intracranial hypertension and intractable, nonspecific headache (ACR 1999)”.

Movement disorder (chorea)

Although a number of movement disorders have been reported in SLE, the ACR case definitions accepts only chorea and it is the most common of these disorders (ACR 1999). It is recognized in less than 2% of cases and appear early in the course of illness and resolve

regardless of treatment (Kovacs et al 1993). It may be unilateral or generalized and is often accompanied by other focal neurologic signs or by changes in mental status. APLs are present in many SLE patients with chorea. The features in imaging and histopathological studies indicate abnormalities in basal ganglia, but it is not yet clear whether chorea is a result of antibody-induced neuronal dysfunction or due to vascular insult (Jennekens & Kater 2002).

Myelopathy

Spinal cord disease is rare but well-described complication in SLE. Transverse myelitis is seen in less than 1% of patients and is characterized by the development of paraplegia, associated with back pain and sensory loss. It is usually seen in late course of the illness and carries a poor prognosis. Vasculitis is a prominent feature of the spinal cord on post-mortem. There has been an association with APL suggesting that the symptom might result from a coagulopathy or antibodies cross-react with spinal cord phospholipids. Atleast 25% of patients who have myelopathy tend to develop optic neuropathy, frequently bilateral (Devic`syndrome). Secondary causes of myelopathy in SLE include an epidural or paraspinal abscess, epidural or subdural hematoma, disc herniation, and intramedullary or extramedullary tumor (Kovacs et al 1993; Liang et al 1994; Brey 2000; Jennekens & Kater 2002).

Seizure disorders

Seizures are part of the revised ACR classification criteria for SLE. Prevalence of 8% to 35% has been reported in SLE patients, although fatal status epilepticus is rare. Seizures are usually generalized but focal seizures have also been documented (McCune et al 1988; Kovacs et al 1993; Brey et al 2002, Sanna et al 2002). They may antedate a diagnosis of SLE by years or be the first manifestation of the disease (Liang & Karlson 1996). APLs have been found with increased frequency in SLE patients with epilepsy. The aetiology of seizures may be an APL-associated cerebral infarction (Brey 2000). In a study of 519 patients, 60 (11.7%) patients suffering with epileptic seizures were identified and all seven patients who presented with recurrent seizures had antiphospholipid syndrome (Appenzeller et al 2004).

Acute Confusional state

The term organic brain syndrome is commonly used to define disturbed mental functioning with delirium, emotional inadequacy, impaired memory or concentration, incoherent speech and increased or decreased psychomotor activity in the absence of any secondary causes (Kovacs et al 1993). The incidence of organic brain syndrome has varied between 2-35% (Estes & Christian 1971; Grigor et al 1978; How et al 1985; van Dam 1991). The disturbances characteristically develop over

hours to days and tend to have fluctuating course (ACR 1999). Metabolic abnormalities such as hypoxia and electrolyte abnormalities should be evaluated and corrected, CNS infection and hypertensive encephalopathy should be excluded (Liang & Karlson 1996; Hanly et al 2005).

The term ‘acute confusional state’ is corresponding to the term ‘delirium’, and according to the ACR nomenclature it ought to be used as a replacement for the term ‘organic brain syndrome’. ACR criteria includes “disturbed level of consciousness or arousal and acute or subacute alteration in cognition and/or a change in mood, affect or behavior. If only deficits in cognition exists and not other features it must be diagnosed as ‘cognitive dysfunction’ (ACR 1999)”.

Depression

It is the most frequently observed psychiatric disorder in SLE with a prevalence rate of about 16-51 %. Mood disorders might be owing to SLE disease activity or as a result of stress due to chronic illness.

Role of steroid in causation of depression cannot be declined. In a study by Gift et al he found significantly higher scores of self reported depression amongst patients suffering from chronic obstructive pulmonary disease on prednisone than patients who were not on steroid therapy.

In a review by Ganz et al, depressive symptoms were found to be twice as common as organic symptoms and seven times as common as schizophreniform symptoms. 13 systemic lupus erythematosus patients had pure depressive symptoms and 11 patients had depressive symptoms mixed with schizophreniform or psychophysical or both but no evidence of organic symptoms.

Mood disorders are associated with poor quality of life, number of hospitalizations and adjustment to illness.

Nery et al evaluated the hypothesis that SLE disease activity is correlated to the presence and severity of major depression. 71 patients were examined for the presence and severity of major depressive disorder, psychosocial stressors, functional disability, SLE disease activity and cumulative damage. Patients suffering from major depression had greater severity of disease activity compared to those without it. Depression was also accompanied by life events and severity was directly correlated with disease activity as well as functional disability.

Anxiety

Anemia, elevated CRF, HPA dysregulation, disfiguring skin rash, scarring alopecia and autoimmune thyroid dysfunction forms the base for

association between SLE and anxiety. The close association of anxiety and depression wherein both coexist makes it more in point.

A study was done by Lindal et al among patients with systemic lupus erythematosus in Iceland and he found the most common disorder to be phobia (56 %), followed by generalized anxiety disorder (12%). Social phobia, Agoraphobia with and without panic and alcohol abuse were commonly found in SLE patients compared to population sample. This study concluded that perhaps high incidence of phobia might be related to disfiguring skin rashes in turn leading to social withdrawal.

Psychosis

Psychosis has been known to be accompanying SLE and SLE is considered as a differential diagnosis for acute psychosis in second decade of life. Reported prevalence varies from 2- 7% . Besides being etiologically related to psychosis these patients also encounter the risk of corticosteroid induced psychosis.

A study was done by Appenzeller et al to evaluate for frequency and risk factors of acute psychosis in SLE patients and to identify clinical as well as laboratory variables useful to differentiate acute psychosis as a primary manifestation of central nervous system from corticosteroid induced psychosis. 537 consecutive SLE patients were studied and

followed. They identified acute psychosis in 89 patients, among them 59 had psychosis primary to central nervous system involvement, 29 were owing to corticosteroids and 2 were not related either to SLE or any other medications. Amongst 59 patients psychosis which was secondary to SLE at illness onset was seen in 19 of them and it was found to be associated with disease activity. During follow up psychosis was observed in 40 patients and it was associated with positive antiphospholipid antibodies. 28 patients had who were on corticosteroid therapy had nearly 38 episodes of psychosis, all of them had severe disease activity and all were on prednisone in doses varying from 0.75 to 1mg/kg/day. Psychosis remitted once prednisone dose was tapered.

A review was done by Lewis DA et al to find the association between corticosteroid therapy and psychosis. He reviewed 79 cases from literature, 14 unreported steroid induced psychiatric syndromes and 29 studies of clinical efficacy of steroids in medical illness. Findings indicated that psychiatric manifestations occur in around 5% of patients with corticosteroid therapy and most of them had affective and/or psychotic symptoms. Female sex, systemic lupus erythematosus and high doses of steroid could be risk factors.

Cognitive Dysfunction

The prevalence of cognitive abnormalities in SLE patients varies widely from 21-66% and is most probably due to differences in selection of patients and case-definition. Various neuropsychological tests have been used to assess nervous system integrity and various studies have been done, the important consistent finding in these studies has been that cognitive impairment is significantly more frequent in SLE patients than in matched samples of healthy subjects or other patients with systemic disease. In addition to this throughout the studies, subclinical cognitive impairment was detected. Even in the absence of overt NP symptoms few SLE patients were found to have significant cognitive problems. No specific pattern of cognitive dysfunction has been found for SLE but as reported in most studies deficits are found in attention and concentration, mild verbal memory, decreased verbal fluency, decreased psychomotor speed and executive dysfunction (Denburg et al 1993; Hanly et al 1998). Studies which used ACR case definitions have detected cognitive dysfunction to be between 52%-78% and cognitive functions were tested by neuropsychological instruments.

Cognitive impairment in SLE patients is assumed to reflect CNS dysfunction. Possible etiology of cognitive disorder have been thought to be an antibody-mediated effect on neuronal functioning or small-vessel

vasculopathy. (Denburg et al 1993; Denburg et al 2003; Hanly 2004). Many studies have been done to analyze the association between cognitive dysfunction and other clinical features but no aforementioned association was found. Presence of other overt neuropsychiatric symptoms anytime during the course of illness or during neuropsychological assessment is linked with cognitive impairment. Psychiatric disorders comorbidity have been found to be around 40 % in SLE patients with cognitive dysfunction. Manifold controversies exist regarding the usage of corticosteroids beyond cognitive dysfunction but most studies did not report such association. According to ACR nomenclature, criteria for diagnosis of cognitive dysfunction includes documentation by neuropsychological testing (documented impairment in one or more of the cognitive domains : simple attention, complex attention, memory, language, reasoning / problem solving, visuo-spatial processing, psychomotor speed and executive functions) and a significant decline with a former level of functioning.

Peripheral nervous system

Peripheral nervous system (PNS) manifestations are not studied extensively in SLE. The reported frequencies of abnormalities varies between 2% and 27% but when patients were evaluated using clinical electromyography and nerve conduction velocity studies, in upto 47% of

SLE patients clinical and subclinical peripheral nerve abnormalities were detected (Estes & Christian 1971; Feinglass et al 1976, Gibson & Myers 1976; Grigor et al 1978; Omdal et al 1988; Hermosillo-Romo et al 2002). Most common peripheral neuropathy in SLE is a mild and symmetric distal sensory or sensorimotor neuropathy. This deficit is progressive over time but might fluctuate and may even be reversible (Goransson et al 2006). In most patients, biopsy and electrodiagnostic findings shows features of vasculitic neuropathy (Rosenbaum et al 1996). Peripheral neuropathy is associated with renal failure and cutaneous vasculitis and it is also considered as an important prognostic factor for mortality in SLE (Hermosillo-Romo et al 2002).

Despite having normal results in clinical evaluation and nerve conduction studies some patients tend to have these neuropathic symptoms. Small nerve fibers like C fibers convey perceptions of warmth and burning pain and A alpha fibers convey cold and sharp pain, a pure small-diameter nerve fiber neuropathy may be responsible for this. The most favourable method for proving the diagnosis of small fiber neuropathy is not established; measurement of heat-pain thresholds or warmth-detection thresholds and quantitative estimation of epidermal nerve fibers have been used. (Omdal et al 2002; Goransson et al 2006)

Acute ascending paralysis (the Guillan-Barre syndrome) has been reported in less than 1%; chronic inflammatory demyelinating polyneuropathy has also been linked to SLE.

Mononeuritis multiplex in SLE is rare and almost always accompanied by evidence of active disease in other organs, although sometimes it may be the presenting feature of the disease (Martinez-Taboada et al 1996).

Carpal tunnel syndrome may be the most common peripheral nerve complication of SLE.

Cranial nerve syndromes have been reported in 3-16% of SLE patients (Estes & Christian 1971; Feinglass et al 1976; Gibson & Myers 1976; Grigor et al 1978). Optic neuropathy occurs in about 1% of patients and in some cases found to be in association with myelopathy. No particular clinical pattern predominates; visual loss, pain and visual field defects may appear. Vasculitis or small vessel disease are suggested as an etiology for optic neuropathy in SLE. Other cranial nerve disorders seen in SLE include trigeminal neuralgia and facial neuropathy (Rosenbaum et al 1996, Jennekens & Kater 2002).

Myasthenia gravis is an autoimmune disorder which is mediated by antibodies to acetylcholine receptors and it may co-occur with other

diseases of immunologic origin and has been diagnosed in patients with SLE but is rare (Rosenbaum et al 1996; ACR 1999).

Quality of life in SLE

Measuring quality of life is an important construct in evaluating disease morbidity and treatment outcome. There are many measures which are disease specific like Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), Systemic Lupus International Collaborating Clinic (SLICC), Systemic Lupus Activity Measure (SLAM) and are based on assessing disease activity by physician. They are primarily used for research plan and do not signify the social impact of disease or useful in measuring functioning and well being of the patients.

A study was done by Jolly M et al to analyse the health related quality of life (HRQOL) of patients with systemic lupus erythematosus in comparison with other chronic diseases. He used self administered medical outcomes study short form-36 (SF-36) questionnaire in 90 patients with systemic lupus erythematosus and in patients with other chronic illnesses like hypertension, adult onset diabetes mellitus, congestive heart failure (CHF), myocardial infarction and depression and it was done in general US population. He found that SLE patients were younger compared to patients of other chronic diseases except for depression. SLE patients scored significantly less than age matched

norms in all 8 domains, their quality-of-life was found to be significantly worse than patients with other chronic illnesses. CHF patients were no worse than SLE in regard to physical function, emotional as well as physical roles and vitality and they were significantly better in bodily pain, social functioning, mental health, and general health compared to SLE patients. Patients who suffered from depression scored low in role emotional and mental health domains but scored better in other domains compared to SLE patients. Systemic lupus erythematosus patients had significantly lower general health compared to other groups. Health related quality of life (HRQOL) was found to be worse significantly and at an early age all domains were affected compared to other patients with chronic diseases.

In a study done by Lim LC et al he found significant correlation between disease activity and psychiatric morbidity among patients with SLE in Singaporean population. Severity of arthritis, myalgia and dermatological lesions were important factors, disease related psychological stress contributed significantly to psychopathology.

A study was done using world health organization quality-of-life-BREF (WHOQOL-BREF) by Khanna S et al in 73 SLE patients and activity of disease was quantified using Mexican Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI). Higher disease

activity scores were seen in association with lower QOL scores in physical and psychological domains but no such correlation were found in social and environmental domains. Physical as well as psychological domains were impaired in active lupus whereas social and environmental domains did not correlate with disease activity. Age or duration of illness did not affect the quality of life in any of the domains.

3. AIM & OBJECTIVES

AIM

To study the psychiatric manifestations in patients with systemic lupus erythematosus.

OBJECTIVES

1. To assess psychiatric manifestations such as anxiety, depression, psychotic symptoms and cognitive functioning among patients with systemic lupus erythematosus.
2. To understand the clinical correlates of the psychiatric manifestations among patients with systemic lupus erythematosus.
3. To assess the quality of life among these patients.

NULL HYPOTHESIS

1. There is no significant difference between the presence of psychiatric manifestations among patients with systemic lupus erythematosus and normal healthy controls.
2. There is no impairment in the quality of life in both the groups.
3. There is no relationship between clinical characteristics, psychiatric morbidity and quality of life in both the groups.
4. There is no difference between the socio demographic data in both the groups.

4. METHOD AND MATERIALS

STUDY DESIGN

A case control design was used in this study.

CASES

Fifty consecutive patients with systemic lupus erythematosus attending the Rheumatology outpatient department at the Government General hospital, Chennai.

INCLUSION CRITERIA

(1) Male and female patients attending the outpatient Rheumatology department, Government General Hospital, Chennai with a definitive diagnosis of systemic lupus erythematosus as per ACR classification 1999.

(2) Participants between 18-60 years of age

(3) Willing to provide informed consent for the participation in the study

EXCLUSION CRITERIA

(1) Patients with other co-morbid physical illnesses such as diabetes, hypertension, infection, etc.

(2) Patients with overlap syndrome.

(3) Patients with known psychiatric illness before the onset of SLE.

(4) Patients with a family history of psychiatric illness.

(5) Refusal to participate in the research.

(6) Refusal to provide informed consent for participation

All the patients were given a thorough physical, neurological and psychiatric examination.

CONTROLS

Fifty healthy individuals from the relatives of the patients with systemic lupus erythematosus from a similar socio-economic background were recruited as the control group. Controls were also evaluated with physical, neurological and psychiatric examination. At recruitment, these controls were matched with the patients with SLE for age, gender and economic background.

Both patients and controls were given the following measures.

MATERIALS USED

A) Semi structured proforma to elicit socio economic and other information such as past history, family history, personal history, premorbid personality details, and clinical history

B) MINI PLUS – structured clinical interview to assess psychiatric morbidity based on DSM IV.

C) Hamilton Anxiety Rating Scale (HAM-A)

D) Hospital Anxiety and Depression Scale (HADS)

E) Hamilton Depression Rating Scale (HAM-D)

F) Brief Psychiatric Rating Scale (BPRS)

G) The Mini-Mental State Examination (MMSE)

H) The Clock Drawing Test (CDT)

I) World Health Organization Quality of Life (WHO QOL) BRFF

TYPE OF STUDY

Comparative study utilizing a case control design

PERIOD OF STUDY

May 2012 to October 2012

PLACE OF STUDY

Department of Rheumatology

Rajiv Gandhi Government General Hospital

Madras Medical College and Research Institute, Chennai

ETHICAL COMMITTEE

The study was approved by the Institutional Ethical Committee, Madras Medical College vide letter No. 04082012

All subjects (both patients and control group) gave informed consent for participation in written form. For those who were illiterate, consent form was read to them and they were requested to put their thumb impression, if they consent for participation.

STATISTICAL ANALYSIS

The data collected from patients and controls were entered into an excel sheet. The data was analyzed using the computer software package developed by WHO and CDC (Epi Info 7, 2012). Continuous variables such as age, duration of treatment, dosage, scores in various rating scales used in study were expressed as mean ± standard deviation (SD). The categorical variables such as gender, education, occupation, income, marital status, family type, residence were represented as frequencies. A descriptive analysis was carried out for certain variables in the patient group.

An independent sample ‘t’ test and ‘chi’ square test were used respectively for the comparative analysis of continuous and categorical variables between the two groups. Pearson's product-moment coefficient was used to understand the linear relationship between two continuous set of variables. For this study, significance level was set at $p < 0.05$.

SCALES and MEASURES USED IN THE STUDY

1. M.I.N.I PLUS NEUROPSYCHIATRIC INTERVIEW

It is a short structured clinical interview which has 20 separate modules for each disorder and is used to diagnose axis I disorders according to DSM IV or ICD 10 developed by Sheehan et al. It has been validated and reliability has been studied in comparison to the "SCID-P (structured clinical Interview for DSM IV)" and the "CIDI (Composite international Diagnostic Interview)" which is a structured interview developed by the World Health Organization for lay interviewers for ICD-10. It has a high inter-rater reliability and validity. It is a clinician administered scale and can be completed within 15minutes. M.I.N.I. Plus is divided into modules identified by letters with each letter corresponding to a diagnostic category. There are screening questions corresponding to the main criteria at the beginning of each diagnostic module except for psychotic disorders. Diagnostic box at the end of each module is given to indicate whether diagnostic criteria are met or not.

2. MINI MENTAL STATE EXAMINATION

Mini–mental state examination (MMSE) or Folstein test is a 30-point questionnaire introduced by Folstein et al in 1975 used to screen for cognitive impairment. It is commonly used to screen for dementia and

also to estimate the severity of cognitive impairment and to follow the course of cognitive changes in an individual over time and serves as an effective way to monitor an individual's response to treatment. It is effective as a screening tool for cognitive impairment with older, community dwelling, hospitalized and institutionalized adults. It is also used as a research tool for screening cognitive disorders in epidemiological studies and follow cognitive changes in clinical trials.

It has 11-questions which measures five areas of cognitive function including orientation, registration, attention and calculation, recall and language. Maximum score is 30, a score of 23 or lower is indicative of cognitive impairment. It takes around 10 minutes to administer and is easy to use repeatedly and routinely.

It relies primarily on verbal response and reading and writing and as a result certain groups of people perform poorly even when their cognition is intact. They include patients who are hearing and visually impaired, intubated, have low English literacy or those with other communication disorders.

3. WORLD HEALTH ORGANISATION QUALITY OF LIFE SCALE-BREF SCALE (WHOQOL-BREF)

"It is a 26-item version of the WHOQOL-100 based on a four domain structure which includes physical, psychological, social and environmental well being". The facets are defined as those aspects of life that have contributed to a person's quality of life. Among 26 items, 24 make up the 4 domains of physical health (7 items), psychological health (6 items), social relationships (3 items) and environmental (8 items) and the rest 2 items measure overall QOL and general health. It uses a Likert type five point scale to assess the patient's response, 24 of 26 questions are used to calculate. Raw scores on each domain are converted to transformed scores using an algorithm, first transformation converts scores to range from 4-20 and second transforms to 0-100 scale comparable with WHOQOL-100. All four domains demonstrate good internal consistency and test-retest reliability. The physical and psychological domains in particular demonstrate good construct validity.

4. HOSPITAL ANXIETY AND DEPRESSION SCALE

This is a self report scale developed by Zigmond and Snaith (1983) for use in hospital populations. It is a reliable tool for detecting symptoms of depression and anxiety in medically ill patients. It focuses mainly on subjective disturbance of mood rather than physical symptoms and

distinguishes psychiatric presentations from physical illness. Depressive subscale includes mostly symptoms of anhedonia and autonomic anxiety. Anxiety and depressive subscales are a valid measure of the severity of the emotional disorder.

It contains of 7 items in each of the two scales and measures anxiety and depression which the patients experienced over the last one week. Each item in the scale has 4 scores from 0 to 3. Scores range from 0-21 and graded as “0-7 = normal, 8-10 =mild, 11-14 =moderate, 15-21= severe”. Because of its ease, speed and acceptability it has been widely used in a variety of clinical populations where depression and anxiety might co-exist with physical illness.

5. HAMILTON RATING SCALE FOR DEPRESSION (HAM-D)

Popularly known as HAM-D, the scale consists of several item questionnaire used to assess depression and as a tool to evaluate recovery from depression. It was devised by Max Hamilton in 1960. The rating scale is intended for adults and used to grade the severity of depression. It was reported to be the gold standard in assessing depression on clinical grounds. Subsequently it was criticized by many researchers since it emphasises more on insomnia than the suicidal ideas or gestures. The original version consisted of 17 items (HSRD-17) the recent version consists of 21 questions.

Scoring patterns:

“0-7 = Normal

8-13 = Mild Depression

14-18 = Moderate Depression

19-22 = Severe Depression

≥ 23 = Very Severe Depression”

6. HAMILTON RATING SCALE FOR ANXIETY (HAM-A)

Abbreviated as HAM-A, the rating scale consists of several item questionnaire used to assess anxiety and as a tool to evaluate recovery from anxiety. It was devised by Max Hamilton in 1959. It was one of the first rating scales to be published and it remains the widely used and well-validated tool by psychiatrists. It should be administered by an experienced clinician. The time taken to administer is 10 to 20 mins, clinician must choose the possible replies to each question by questioning the patient and by detecting the patient's symptoms. The HAM-A probes 14 parameters, each item is scored on a 5-point scale, ranging from 0=not present to 4=severe. The Sensitivity is 85.7% and the Specificity is 63.5%.

Scoring patterns

0-13→normal

14-17 →mild anxiety

18-24→moderate

>25→severe

7. BRIEF PSYCHIATRIC RATING SCALE (BPRS)

Is considered to be one of the oldest rating scales to measure psychosis and it was first published in 1962. The Brief Psychiatric Rating Scale (BPRS) is an inclusive 24-item symptom scale. The BPRS is used as part of a clinical interview in which the clinician makes observations amongst several symptomatic criteria and depends upon patient self-report for other criteria.

Items 1 through 14 are rated based on patients self-report during the clinical interview. Symptoms not assessed are marked as “NA.” Items 7, 12 and 13 are also rated on observed behavior during the interview. Items 15 through 24 are rated based on the patient’s observed behavior or speech during the interview.

5. RESULTS AND DISCUSSION

5.1 Descriptive analysis of the patient group

5.1.1 Socio-demographic characteristics of the patients with systemic lupus erythematosus

Table 1: Socio-demographic characteristics of the patients with systemic lupus erythematosus (n=50)

	Socio demographic characters	No of patients	Percentage
GENDER	Male	2	4 %
	Female	48	96 %
MARITAL STATUS	Married	28	56 %
	Unmarried	15	30 %
	Others	7	14 %
EDUCATION	Illiterate	4	8 %
	Primary	5	10 %
	Middle	8	16 %
	High	23	46 %
	Intermediate	3	6 %
	Graduation/post-graduation	7	14 %
OCCUPATION	Unemployed	40	80 %
	Unskilled	2	4 %
	Semiskilled	2	4 %
	Semi-profession	5	10 %
	Profession	1	2 %
INCOME	<1000	1	2 %
	1000-2999	11	22 %
	3000-4999	21	42 %
	5000-7499	16	32 %
	7500-9999	1	2 %
RESIDENCE	Urban	43	86 %
	Rural	7	14 %
FAMILY TYPE	Joint	11	22 %
	Nuclear	39	78 %

The above table shows that the sample comprises of predominantly females 96 % and 4 % are males. Among them majority are married 56 %, 30 % are not married, and 14 % are either separated, divorced or widow. Most of them have reached high school level of education (46 %), few are graduated (14%). Most of the subjects (80%) are housewives. Most of them have a monthly income of less than 5000 (42%). Majority of the patients with SLE belong to urban background (86%) and most of them live in nuclear families (78%).

5.1.2 Clinical characteristics of the patients with systemic lupus erythematosus

Table 2: Description of clinical data in patients with systemic lupus erythematosus

Clinical variables	No of patients	Mean	Standard deviation	Median
Duration of illness	50	1.94	0.7	2
Current dose of corticosteroids	50	11.5	12	6.25
Highest dose of corticosteroids	50	27.9	18.2	20

The above table shows that the mean duration of illness is 1.94 years; and SLE patients received a mean dose of 11.5 mg corticosteroids with a mean highest dose of 27.9 mg corticosteroids. Most patients were treated with immunosuppressant drugs like cyclophosphamide, azathioprine along with corticosteroids prednisone.

5.1.3 Psychiatric manifestations as elicited by MINI plus neuropsychiatric interview

Both patients and control group were given MINI PLUS neuropsychiatric interview to assess psychiatric morbidity based on DSM IV. None of the people in control group qualified for DSM IV diagnosis. Among patient group 16 (32%) qualified for a diagnosis of anxiety and 26 (52%) qualified for a diagnosis of depression. Their symptoms were quantified using various rating scales as illustrated below.

5.1.4 Psychiatric manifestations - anxiety and depression among patients with systemic lupus erythematosus

Figure 1: Hospital anxiety and depression scale-anxiety score (HADS-A)

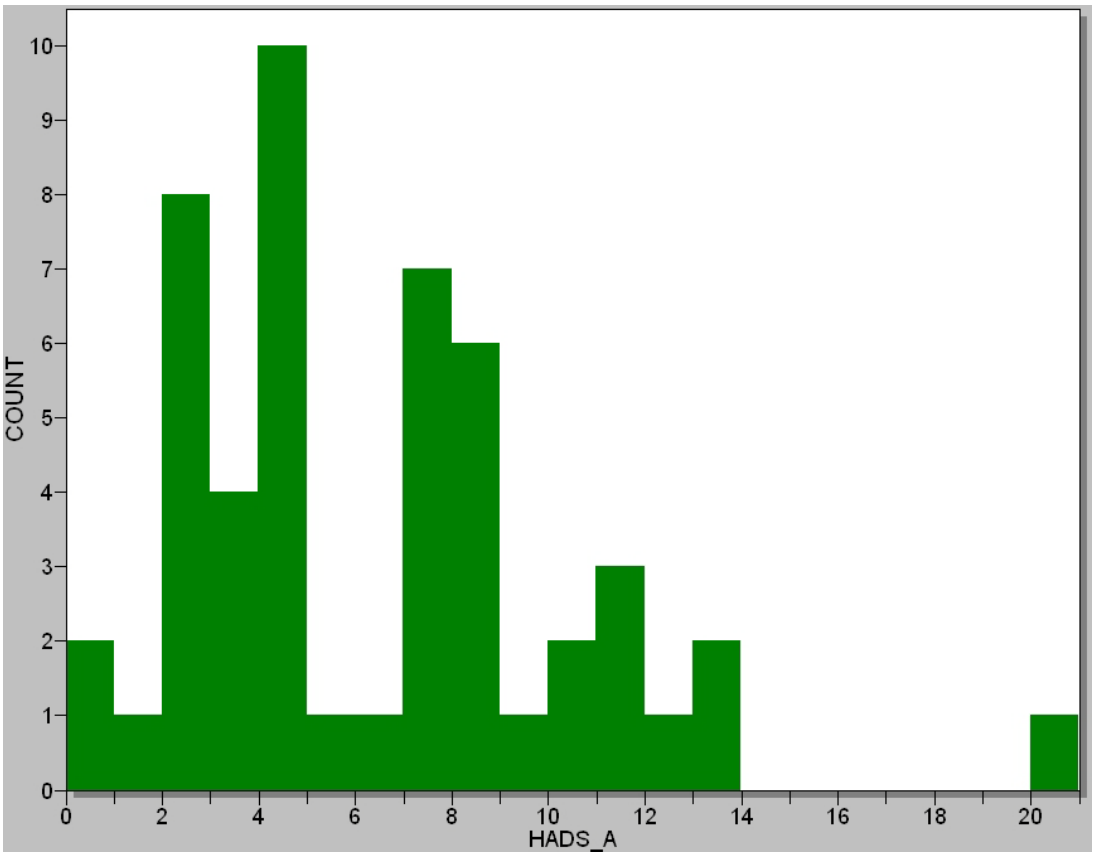


Table 3: Frequency Distribution of individual scores in HADS-A

HADS-A	0 score in %	1 score in %	2 score in %	3 score in %
Tension	22	54	20	4
Frightful	50	18	26	6
Worrying	20	36	38	8
Relaxation	20	38	38	4
Butterflies in stomach	56	24	14	6
Restless	36	44	20	4
Panic	36	38	20	8

As evaluated by Hospital Anxiety And Depression Scale-anxiety subscale (HADS-A) and depicted in figure 1 and table 3 patients scored high on questions which reported being tensed and frightened as if something awful is about to happen, having worrying thoughts most of the time, feeling restless and unable to sit at ease and feel relaxed.

Figure 2: Hospital anxiety and depression-depression scores (HADS-D)

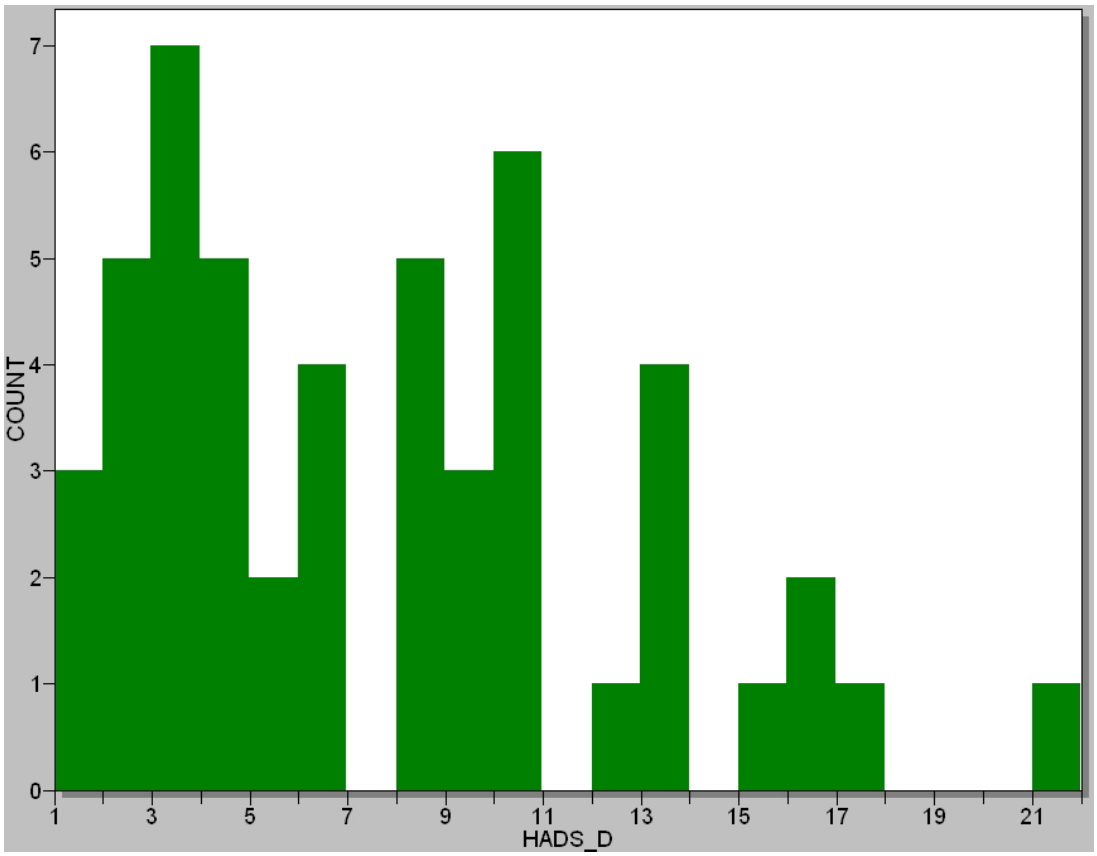
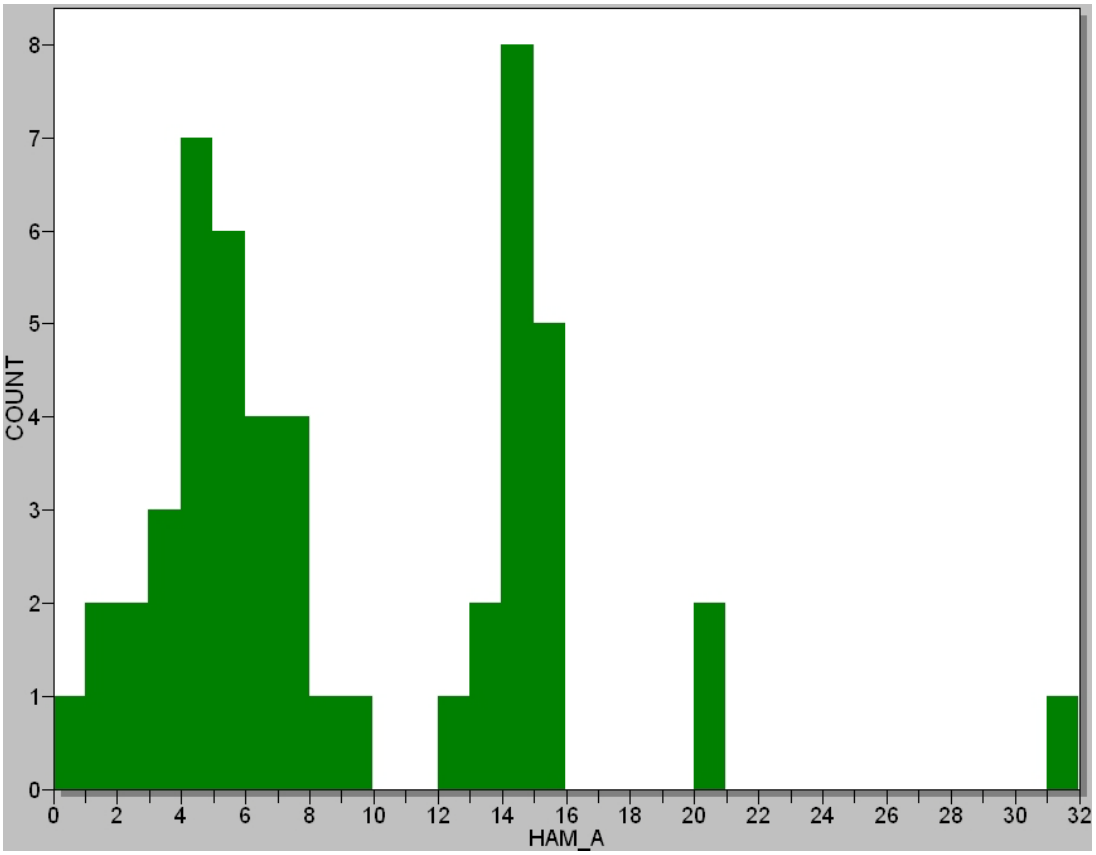


Table 4: Frequency Distribution of individual scores in HADS-D

HADS-D	0 score in %	1 score in %	2 score in %	3 score in %
Enjoyment	22	36	34	6
Laughing	32	36	26	6
Cheerful	38	36	20	6
Slowed down	0	24	42	34
Lost interest in appearance	30	38	16	16
Enthusiasm	36	42	12	8
Entertainment	40	22	32	6

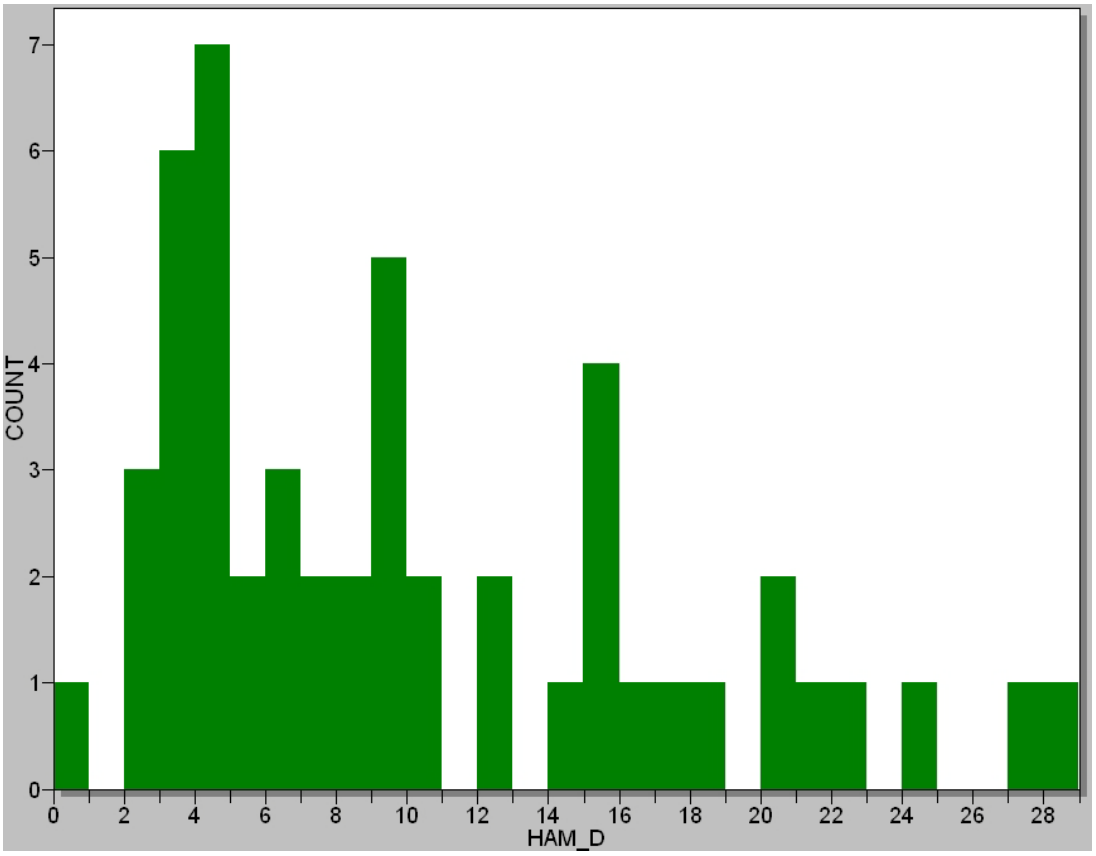
As assessed by Hospital Anxiety And Depression Scale-Depression subscale (HADS-D) and depicted in figure 2 and table 4 patients scored high on questions which reported that they can't enjoy the things which they once enjoyed and don't feel cheerful most of the time, they feel as if they are slowed down very often and have no interest in their appearance and don't take as much as care they should.

Figure 3: Hamilton anxiety scale (HAM-A)



As depicted in figure 3 and rated by Hamilton Anxiety Scale (HAM-A) most of them had mild anxiety and one person had severe anxiety. They scored high on questions like having anxious mood, feeling tensed, suffering from somatic complaints like muscle aches or pains, cardiovascular symptoms like tachycardia, palpitations and autonomic symptoms like sweating, dry mouth.

Figure 4: Hamilton depression rating scale (HAM-D)



As depicted in figure 4 and rated by Hamilton depression rating scale (HAM-D) a proportion of patients (N = 11) had mild depression and more (N =15) had moderate to severe level of depression. They scored high on questions like having depressed mood, ruminating over past errors or sinful deeds and feeling present illness is punishment, having suicidal ideas, suffering from insomnia, difficulty in carrying out activities, loss of concentration, worrying about minor matters and somatic symptoms.

Table 5: Frequency distribution of symptoms by rating scales (HAM-A & HAM-D)

Rating Scales	Absent	Mild	Moderate	Severe	Total
HAM-A	34	13	2	1	50
HAM-D	24	11	8	7	50

The above table shows that 13 patients had mild anxiety (26 %), 2 suffered from moderate level of anxiety (4%) and 1 had severe anxiety (2%) as rated by Hamilton anxiety scale (HAM-A). As rated by Hamilton depression rating scale (HAM-D) 11 have mild depression (22%), 8 had moderate depression (16%) and 7 patients suffered from severe depression (14%).

Table 6: Frequency distribution of symptoms by rating scale (HADS)

	Normal	Borderline Abnormal	Abnormal	Total
HADS-A	34	9	7	50
HADS-D	26	14	10	50

The above table shows that 16 patients (32%) had abnormal scores on anxiety scale in Hospital Anxiety and Depression Scale (HADS-A) and 24 patients (48%) had abnormal scores on depression scale (HADS-D).

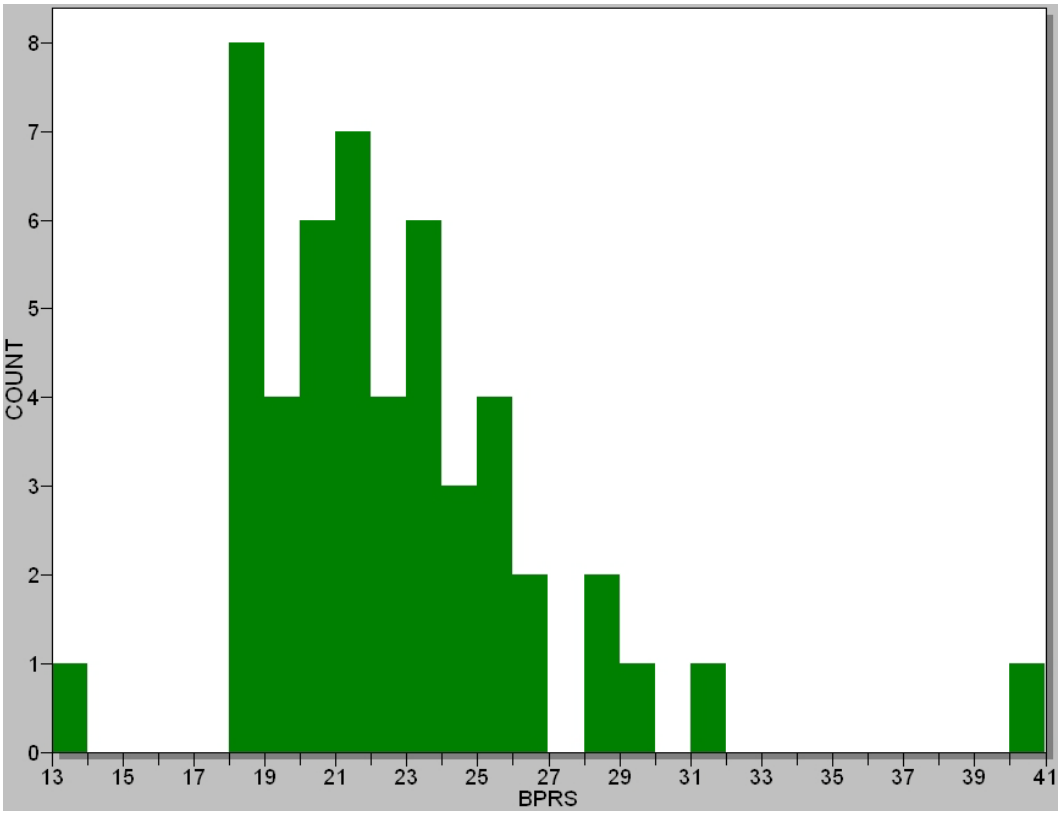
Table 7: Systemic lupus erythematosus patients subdivided on the basis of HAM-A and HAM-D SCORES

	HAM-A		
HAM-D	**Absent**	**Mild**	**Significant (Moderate + Severe)**
Absent	19	5	0
Mild	8	3	0
Significant (Moderate + Severe)	7	5	3

The above table shows that among these 50 patients, mixed anxiety and depression as elicited by Hamilton rating scales is not uncommon. Just more than a fifth of the patients with SLE (22%) have mixed anxiety and depression symptoms to a mild or significant level. Six percent of the patients have significant mixed anxiety and depression.

5.1.5 Psychiatric manifestations – psychotic symptoms among patients with systemic lupus erythematosus

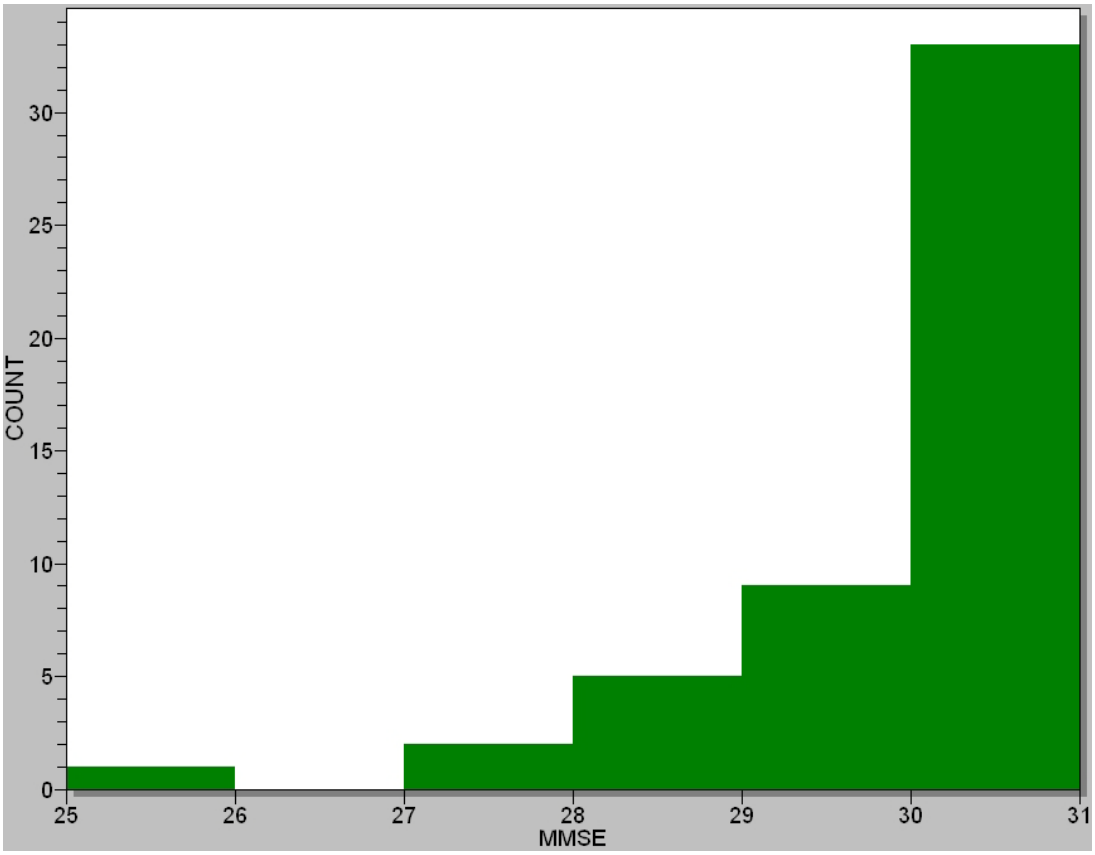
Figure 5: Brief Psychiatric Rating Scale



As depicted in figure 5 and rated by brief psychiatric rating scale (BPRS) no frank psychotic symptoms were elicited and patients scored in questions such as somatic concern and preoccupation with physical health, anxiety, guilt feelings, tension, depressive mood.

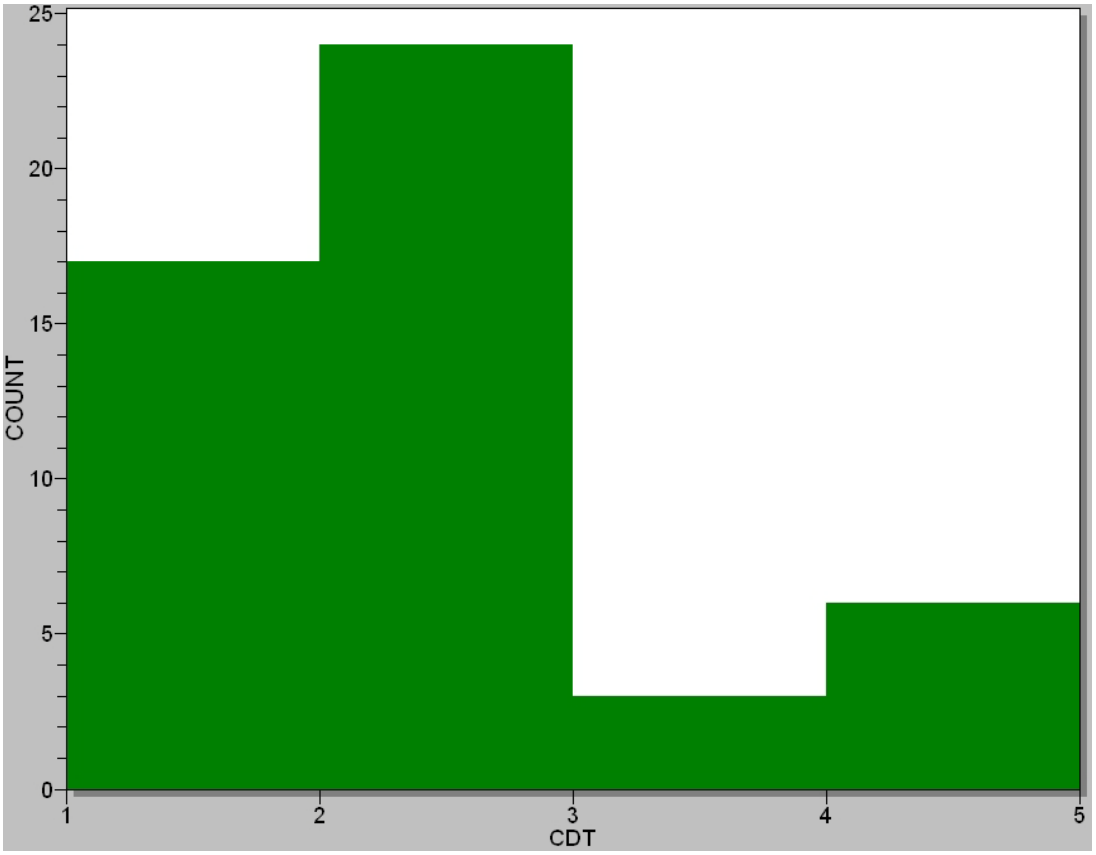
5.1.6 Psychiatric manifestations – cognitive functioning among patients with systemic lupus erythematosus

Figure 6: Mini Mental Status Examination



As rated by Mini Mental State Examination (MMSE) and depicted in figure 6 none of them scored below the cut off score of 23. It was observed that many patients had difficulty in copying the pentagon and impairment in recalling given objects, recalled either 1 or 2 objects out of 3.

Figure 7: Clock Drawing Test Scores



As depicted in figure 7 and assessed by clock drawing test (CDT) and rated by scoring given by Shulman et al 1993 a score of 3 or more represented a cognitive deficit and in this sample, 18 % patients had cognitive impairment.

5.2 Relationship between clinical data and psychiatric manifestations

5.2.1 Relationship between clinical data and anxiety and depression

Table 8: Correlation coefficients of Clinical data with anxiety, depression and cognition

Clinical data	Rating scales	Correlation coefficient	'p' value
Duration of illness	HADS A	0.0	0.7972 NS
	HADS D	0.01	0.5924 NS
	HAM A	0.01	0.5499 NS
	HAM D	0.0	0.8866 NS
	CDT	0.03	0. 2160 NS
	MMSE	0.02	0.3641 NS
Current dose of corticosteroids	HADS A	0.0	0.6461 NS
	HADS D	0.04	0.1662 NS
	HAM A	0.0	0.7874 NS
	HAM D	0.05	0.1316 NS

The above table demonstrates that clinical data such as duration of illness (SLE) and current dose of corticosteroids received by the individual does not have any significant association with the anxiety, depression and cognitive functioning elicited by various measures such as HADS, HAM-A, HAM-D, CDT and MMSE. Thus these psychiatric manifestations such as anxiety and depression are not related to clinical variables such as duration of disease and dose of corticosteroids.

5.2.2 Relationship between anxiety, depression and cognitive functioning

Table 9: Correlation coefficients of anxiety, depression and cognition

Anxiety / Depression rating scales	Cognitive functioning rating scales	Correlation coefficient	'p' value
HADS D	CDT	0.05	0.1180 NS
HAM D	CDT	0.04	0.1769 NS
HADS A	CDT	0.00	0.6849 NS
HAM A	CDT	0.01	0.5242 NS

It was revealed that in nine patients the CDT scores were above 3, the cut-off for cognitive impairment. To understand whether the cognitive impairment was associated with the levels of anxiety or depression, correlation between these two sets of variables were carried out. Findings from the above table revealed that the there is no significant association between anxiety, depression as elicited by HADS, HAM-A, HAM-D and CDT scores. Thus the cognitive impairment seen in these patients is independent of anxiety and depression.

5.3 Comparison of patients with SLE and normal controls for demographic and clinical variables

5.3.1 Comparison of cases and controls for demographic variables

Table 10 Comparison of Patients with SLE with normal controls for Gender

Gender	Patients With SLE	Control	Df	'chi' square value	'p'value
Males	2	2	1	0.2604	0.6098 NS
Females	48	48			

Table 11: Comparison of Patients with SLE with normal controls for Age

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	30.7	9.2	0.1658	0.8687 NS
Control	50	31	8.9		

Table 12: Comparison of Patients with SLE with normal controls for Family Type

Family Type	Cases	Controls	df	'chi square value'	'p' value
Joint	11	16	1	1.27	0.26 NS
Nuclear	39	34			

Table 13: Comparison Of Patients With SLE With Normal Controls For Income

INCOME	CASES	CONTROLS	df	'chi square value'	'p' value
<5000	33	24	1	3.3	0.0690 NS
>5000	17	26			

Table 14: Comparison of Patients With SLE With Normal Controls For Residence

RESIDENCE	CASES	CONTROLS	df	'chi square value'	'p' value
URBAN	43	45	1	0.38	0.5382 NS
RURAL	07	6			

Table 15: Comparison Of Patients With SLE With Normal Controls For Marital status

MARITAL STATUS	CASES	CONTROLS	df	'chi square value'	'p' value
MARRIED	28	33	1	1.05	0.3053 NS
OTHERS	22	17			

Table 16: Comparison Of Patients With SLE With Normal Controls For Occupation

OCCUPATION	CASES	CONTROLS	df	'chi square value'	'p' value
EMPLOYED	10	18	1	3.17	0.0747
UNEMPLOYED	40	32			

All subjects in patient group and control group were compared for demographic characteristics such as age, gender, education, occupation, income, marital status, family type and residence. Data analysis demonstrates that there is no statistically significant difference between the two groups for the above variables. This shows that cases and controls are matched for various demographic characteristics.

5.3.2 Comparison of patients with SLE and control group for anxiety and depression

Table 17:
Comparison of Patients with SLE with normal controls for HAM-A scores

Sample	NUMBER	MEAN	SD	't' value	'p' value
Patients With SLE	50	8.8	6.1	3.8	0.0002
Control	50	4.9	3.5		

The above table compares total scores as obtained through Hamilton Anxiety Scale (HAM-A). The mean ± SD (8.8 ± 6.1) score of patients with SLE is greater than the mean ± SD (4.9 ±3.5) of the control group. This difference is significant statistically (p 0.0002). This shows that patients with SLE have more anxiety scores as revealed by HAM-A compared to healthy controls.

Table 18: Comparison of patients with SLE with normal controls for HADS-A scores

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	5.9	4	4.3	0.01
Control	50	3.2	2		

The above table shows that the anxiety scores obtained through Hospital Anxiety and Depression Scale are higher among the patients with SLE compared with normal controls and such a difference between the mean scores is statistically significant (p 0.01).

Increased anxiety disorder among SLE is reported commonly among SLE patients (Bachen et al 2009; Ghaydaa et al 2011; Hawro et al 2011). Elevated anxiety levels among patients with SLE could be attributed to the following factors:

1. SLE is a chronic disease
2. SLE produces skin manifestations inducing anxiety as skin manifestations can cause embarrassment in public
3. The active disease process itself produces neuropsychiatric manifestations including anxiety symptoms

Table 19: Comparison of patients with SLE with normal controls for HAM-D scores

Sample	NUMBER	MEAN	SD	't' value	'p' value
Patients With SLE	50	9.7	7.2	4.1	0.0001
Control	50	5.1	3.1		

The above table compares the total scores as obtained through Hamilton Depression Rating Scale (HAM-D). The mean ± SD (9.7 ± 7.2) score of patients with SLE is greater than the mean ±SD (5.1 ±3.1) of the control group. This difference is significant statistically (p 0.0001). This shows that patients with SLE have more depressive scores as revealed by HAM-D compared to healthy controls.

Table 20: Comparison of patients with

SLE with normal controls for HADS-D scores

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	7.2	4.9	4.3	0.01
Control	50	4.1	2.2		

Comparison of mean scores obtained in HADS- D between the patients with SLE and normal control demonstrates that the scores are higher among patients with SLE and such a difference is statistically significant (p 0.01).

High rates of depression have been reported in many studies in the literature (Purandare et al 1999; Mariana et al 2010). Depression among patients with SLE may be attributable to the following:

1. As a part of the disease
2. Can be caused by various medications (e.g., corticosteroids) used in treating the disease
3. May be a reactive psychological disturbance owing to stress of having a chronic disease.

Table 21: Comparison of patients with

SLE with normal controls for BPRS scores

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	22.1	4.3	4.5	0.01
Control	50	19.2	1.5		

The above table demonstrates that there is statistically significant difference (p 0.01) between patient and control group for psychotic symptoms as elicited by Brief Psychiatric Rating Scale (BPRS). In our sample psychotic symptoms among patients with SLE are infrequent but the elevation in the BPRS scores is primarily due to scores on symptoms such as somatic concern and preoccupation with physical health, anxiety, guilt feelings, tension, depressive mood. The lower frequency of psychotic symptoms is also reported in earlier studies (Purandare et al 1999; Raghavendra et al 2012). Pego-Reigosa and Isenberg in 2008 have reported in their study that psychosis is a rare manifestation of SLE; and it might be an initial manifestation of the disease, usually occurring in the first year of disease in few cases. Psychosis may be associated biological markers of lupus activity like ANA, anti-dsDNA.

Table 22: Comparison of Patients with SLE with normal controls for MMSE scores

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	29.4	1	2.3	0.02
Control	50	29.7	0.4		

The above table shows a statistically significant difference for the total MMSE scores between the patient group and control group (p 0.02). Even though the descriptive analysis has identified that none has scored below the cut-off point of 23, yet compared with healthy controls there is a decline in cognitive functioning among patients with SLE.

Table 23: Comparison of patients with SLE with normal controls for CDT scores

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	1.96	0.9	5.9	0.001
Control	50	1.12	0.3		

Above table shows that the patient group have higher clock drawing test (CDT) scores compared with the control group. (patient's mean 1.96, median 2 : controls mean 1.12,median 1.12). The difference between the 2 groups is statistically significant ($p<0.001$). Compared with

healthy controls patients with SLE appeared to have more cognitive disturbances. Nine of the patients (18%) have scored 3 or more in CDT. Such a decline in cognitive functioning could be due to either disease activity or attributable to psychiatric symptoms such as depression (Melo et al 2012). Hence the CDT scores, depression and anxiety scores in HAM-A and HAM-D were analysed using Pearson correlation coefficient (see table 9). Results show no statistically significant correlation between cognition, anxiety and depression. This concludes that they all are independent variables.

Cognitive functioning decline is often reported among the patients with SLE (Maneeton et al, 2010). Cognitive abnormalities associated with SLE are impairment in immediate, delayed and retrieval of memory, impairment in visuospatial activities, poor attention and concentration, difficulties with abstract thinking and reduction in psychomotor speed (Anselm Mak et al 2009).

5.3.3 Comparison of patients with SLE with normal controls for quality of life

5.3.3.1 Comparison of patients with SLE with normal controls for physical health

Table 24 : Comparison of patients with SLE with normal controls for WHOQOL-DOMAIN 1 scores (0-100)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	49.9	7.45	1.76	0.08 NS
Control	50	52.7	8.57		

Table 25 : Comparison of patients with SLE with normal controls for WHOQOL-DOMAIN 1 scores (4-20)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	11.98	1.22	1.76	0.08 NS
Control	50	12.44	1.38		

This table illustrates that there is no statistically significant difference between the transformed scores on Domain 1 of WHOQOL-BREF scale. This shows that the quality-of-life relating to physical health is not affected in patients with systemic lupus erythematosus and is comparable to normal controls.

5.3.3.2 Comparison of patients with SLE with normal controls for psychological health

Table 26 : Comparison of patients with SLE with normal controls for WHOQOL-DOMAIN 2 scores (0-100)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	47.7	10.2	3.04	0.003
Control	50	53.68	9.2		

Table 27 : Comparison of patients with SLE with normal controls for WHOQOL-DOMAIN 2 scores (4-20)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	11.62	1.63	3.06	0.0028
Control	50	12.58	1.48		

The above table shows statistically significant difference between patient and control group for transformed scores on domain 2 of WHOQOL-BREF scale. This signifies that the psychological domain related quality-of-life is significantly impaired in SLE patients compared with normal controls. Such a finding is consistent with results obtained from other studies (Doria et al 2004; Rinaldi et al 2004).

5.3.3.3 Comparison of patients with SLE with normal controls for social relationships

Table 28: Comparison of Patients with SLE with normal controls for WHOQOL-DOMAIN 3 scores (0-100)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	53.58	17.43	0.53	0.59 NS
Control	50	55.3	14.6		

Table 29: Comparison of Patients with SLE with normal controls for WHOQOL-DOMAIN 3 scores (4-20)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	12.58	2.78	0.54	0.58 NS
Control	50	12.86	2.33		

This table shows no statistically significant difference between the transformed scores on Domain 3 of WHOQOL-BREF scale. This shows that the quality-of-life relating to social relationships are not affected in patients with systemic lupus erythematosus and is in comparison with normal controls.

5.3.3.4 Comparison of Patients with SLE with normal controls for environment

Table 30: Comparison of Patients with SLE with normal controls for WHOQOL-DOMAIN 4 scores (0-100)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	57.18	11.36	0.34	0.73 NS
Control	50	57.92	10		

Table 31: Comparison of Patients with SLE with normal controls for WHOQOL-DOMAIN 4 scores (4-20)

Sample	Number	Mean	SD	't' value	'p' value
Patients With SLE	50	13.12	1.81	0.35	0.72 NS
Control	50	13.24	1.58		

This table shows no statistically significant difference between the transformed scores on Domain 4 of WHOQOL-BREF scale. This shows that the quality-of-life relating to environment is not affected in patients with SLE and is comparable to normal controls.

5.3.3.4 Relationship of Quality of life and psychiatric manifestations in SLE

The quality of life is relatively unaffected amongst the patients with SLE except in the domain of psychological health. A correlation analysis was carried out between the scores on the psychological health domain of the WHOQOL-BREF Scale and the anxiety, depression elicited by various measures used in this study. The findings are shown below.

Table 32 : Correlation Coefficients Of Anxiety, Depression And Quality Of Life

Clinical data	Rating scales	Correlation coefficient	'p' value
Domain 2 scores (1-100)	HADS A	0.29	0.000055 Sig
	HADS D	0.31	0.000030 Sig
	HAM A	0.20	0.000992 Sig
	HAM D	0.11	0.016241 Sig
Domain 2 scores (4-20)	HADS A	0.12	0.013229 Sig
	HADS D	0.11	0.018430 Sig
	HAM A	0.20	0.001023 Sig
	HAM D	0.11	0.016749 Sig

The table demonstrates the significant correlation between psychological domain scores in WHO quality of life scale and the psychiatric manifestations such as depression and anxiety as elicited by HADS,HAM-A, HAM-D. The results are in agreement with data reported

from the study by Doria et al in 2004 in Italy. According to Doria and colleagues impairment of quality-of-life does not depend directly on disease severity or permanent damage but these could lead to the emergence of anxiety and/or depressive symptoms in patients with SLE. Anxiety, depression and joint pain may actually impair the person's quality-of-life.

6. LIMITATIONS

This study had the objective to assess psychiatric manifestations such as anxiety, depression, psychotic symptoms and cognitive functioning among patients with systemic lupus erythematosus. The design employed was case control and used age, gender matched normal healthy volunteers from the relatives as controls. Comparison with normal controls helped to know that the psychiatric manifestations were more frequent in patients with SLE compared with normals. Yet to understand that psychiatric manifestations are more frequent in SLE compared with other chronic diseases, it would have been beneficial to use in addition a control group of another chronic condition such as rheumatoid arthritis. The psychiatric manifestations can be attributed to many factors including disease activity. It would have been useful if detailed clinical and laboratory data related to SLE was gathered; data on disease activity, definition of organ involvement, nuclear and antiphospholipid antibody detection, would have been useful to understand the relationship of psychiatric manifestations with these variables. In this study data was collected on basic clinical data such as duration of illness, type of treatment and dose of corticosteroids and hence there is limitation in the analysis of the relationship of determinants of psychiatric manifestations. Similarly it is learnt from the literature that

cognitive impairment in SLE is often due to direct central nervous system involvement and it can progress with the disease. Only longitudinal data can provide insights into the cognitive functioning and its progression with the disease and modification by treatment. Being retrospective in design, the recall of all events that have occurred in the past can be difficult and recall bias is not uncommon in this type of design. Finally, it should be stated that since the patients with SLE were only recruited from a tertiary teaching medical college hospital outpatient department, the results of the study cannot be generalised to all patients with SLE in the community settings. Despite these limitations, this study has highlighted the clinical importance of assessing the psychiatric manifestations such as anxiety, depression and cognitive functioning and quality of life in patients with SLE.

7. SUMMARY AND CONCLUSIONS

Systemic lupus erythematosus, a multisystem disease has a variable course characterised by exacerbations and remissions; during the course of the illness, psychiatric manifestations are not uncommon. In view of the scarce Indian literature related to the study of psychiatric manifestations among patients with SLE, the present study has the objective of assessing the psychiatric manifestations, in particular, anxiety, depression, psychotic symptoms, cognitive functioning and quality of life among patients with SLE.

A case control design was employed for the study, in which fifty consecutive patients with systemic lupus erythematosus attending the Rheumatology outpatient department at the Government General hospital, Chennai constituted the cases. The control group consisted of fifty healthy volunteers from the family members and relatives of the cases belonging to the same economic group. Care was taken to select controls matched for gender and age.

Both patients and controls were administered a semi structured interview schedule that collected demographic, personal data; in addition relevant clinical data was gathered from the patients with SLE. They were interviewed using MINI PLUS to evaluate for psychiatric morbidity. The cases and controls were administered the following measures: Hamilton

Anxiety Rating Scale (HAM-A); Hamilton Depression Rating Scale (HAM-D); Hospital anxiety and depression scale (HADS); Brief psychiatric rating scale (BPRS); the Mini-Mental State Examination (MMSE); the Clock Drawing Test (CDT); and the World health organization quality of life (WHO QOL) BRFF. Further, the cases were assessed using SLE disease activity index (SLEDAI). The subjects in both the case and control groups provided written consent for participation in the study. The study design and protocol was approved by the Institutional Ethical Committee, Madras Medical College vide letter no 04082012. The data was analyzed using the computer software package Epi 6 Info. Significance level was set at $p < 0.05$.

Among the patients with SLE, most were females (96%), from urban areas (86%), living in nuclear families (76%), married (56%) and educated up to higher secondary level (46%). The mean duration of SLE was about 2 years and the mean current dose of corticosteroids was 11.5 mg (median dose 6.25 mg).

Psychiatric manifestations such as anxiety and depression were frequently reported by patients with SLE. Among them, 26% patients had mild anxiety, 4% moderate level of anxiety and 2% had severe anxiety as rated by Hamilton anxiety scale (HAM-A). As rated by Hamilton depression rating scale (HAM-D) 22% had mild depression, 16% moderate depression and 14% severe depression. Sixteen patients (32%)

had abnormal scores on anxiety scale in Hospital Anxiety and Depression Scale (HADS-A) and 24 patients (48%) had abnormal scores on depression scale (HADS-D). Subdividing based on HAM-A & HAM-D scores, just more than a fifth of the patients with SLE (22%) reported mixed and depression symptoms to a mild or significant level. In this study most patients with SLE did not report significant level of psychotic symptoms. Using Clock drawing test, nine patients (18%) patients had a cut-off score of 3 or more signifying cognitive impairment. The cognitive impairment observed in these patients was independent of anxiety and depression. None of the psychiatric manifestations such as anxiety, depression and cognitive impairment were associated with clinical variables such as duration of illness and dose of corticosteroids.

The patients with SLE were compared with the control group for demographic variables and it was revealed that these two groups did not have statistically significant difference for the following variables: age, gender, marital status, education, income, occupation, family type and residence. Thus the cases and controls were matched for various demographic characteristics. Comparison was made between the two groups for psychiatric manifestations such as anxiety and depression. Anxiety as elicited by HAM-A was elevated in patients with SLE compared with normal controls (8.8 ± 6.1 vs. 4.9± 3.5) and this difference in the means was statistically significant (p 0.0002). Similarly the

difference in the means of anxiety scores in HAM-A between the cases and controls was statistically significant (5.9 ± 4 vs. 3.2± 2; p 0.01). Depression as shown by HAM-D was more in patients with SLE compared with normal controls (9.7 ± 7.2 vs. 5.1± 3.1) and this difference in the means was statistically significant (p 0.0001). Similarly the difference in the means of depression scores in HAM-D between the cases and controls was statistically significant (7.2 ± 4.9 vs. 4.1± 2.2; p 0.01). Higher rates of anxiety and depression have been reported among patients with SLE in several studies (Hawro et al, 2011; Bachen et al, 2009; Purandare et al, 1999; Mariana et al, 2010). Cognitive impairment was more among patients with SLE compared with control group and this is evidenced by greater mean scores in CDT for patients with SLE (1.96 ± 0.9 vs. 1.12± 0.3; p 0.001). Similarly the difference between the mean scores of MMSE was statistically significant between the two groups (p 0.02).

The two groups, patients with SLE and the normal controls were compared for the scores on the four domains – physical health, psychological health, social relationships and environment – in the WHOQOL - BREF scale. It was observed that there was no statistically significant difference between the two groups in three domains namely physical health, social relationships and environment whereas the difference between the two groups in psychological health was

statistically significant (47.7 ± 10.2 vs. 53.7± 9.2; p 0.03). There was significant correlation between psychological domain scores in WHO quality of life scale and the psychiatric manifestations such as depression and anxiety as elicited by HADS, HAM-A, HAM-D.

The study findings indicate that psychiatric manifestations such as anxiety and depression is common among patients with SLW; this is consistent with several studies on psychiatric morbidity among SLE reported from north America, Europe and Africa (Hawro et al, 2011; Kozora et al, 2006; Shehata et al, 2011). In this study clinical data such as duration of disease and dose of corticosteroids do not have a significant association with anxiety and depression. The elevated level of anxiety and depression can be due to multiple factors; disease activity, direct involvement of the central nervous system and psychological reaction, stress of living with a chronic disease have all been proposed as possible reasons for the increased prevalence of anxiety/depression in patients with SLE. Whatever is the cause, the presence of psychiatric manifestations such as depression and anxiety can influence and cause impairment to quality of life among patients with SLE. In this study it is shown that the quality of life in the psychological domain is significantly impaired among patients with SLE compared with normal controls. The strong correlation between the psychiatric manifestations and the impairment to psychological domain of quality of life demonstrates the

significance of anxiety and depression amongst patients with SLE. Given the frequency as well the importance of its contribution to impairment to quality of life, it is suggested that all patients with SLE should be clinically screened for the presence of anxiety and depression. The study findings reveal that anxiety and depression can co-occur together in some of these patients and this should be taken into consideration while assessing patients for psychiatric morbidity.

Cognitive impairment is observed more among patients with SLE compared with normal control; this observation is consistent with earlier studies on this topic (Maneeton et al, 2010). In this present study it is shown that the cognitive impairment is independent of psychiatric manifestations such as anxiety and depression. Earlier studies have observed association between cognitive impairment and disease activity at the onset of the disease. Subclinical involvement is suggested as a reason for the cognitive impairment in patients with SLE. Longitudinal data on cognitive functioning in patients with SLE will help to understand the relationship between cognitive functioning and the disease activity.

It is reported that in patients with SLE disturbance to quality of life does not appear to depend directly on the severity of SLE or permanent damage. On the other hand, the impairment may be attributable to the depressive and anxiety symptoms that may emerge in these patients (Doria et al, 2004). Thus, physicians treating SLE should be cognizant of

the increased prevalence of anxiety/depression among patients with SLE and understand the importance of early identification and treatment of anxiety / depressive symptoms. The physicians treating SLE may be given training to identify anxiety / depression in clinical settings and to provide treatment wherever necessary for patients with significant anxiety/depression. In general hospital settings, consultation-liaison between rheumatology and psychiatry departments will be helpful in delivering appropriate services that would mitigate the psychological distress among patients with SLE.

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APPENDIX I - PROFORMA

A – SOCIODEMOGRAPHIC DATA **RCC NO:**

• Name :

• Age :

• Sex :

• Education : Nil/School/SSLC/HSC/Graduate/PG/Professional

• Occupation : Unemp/Emp/Non-Prof/Prof

• Income :

• Marital Status : Unmarried/Married/Separated/Divorced/Widow

• Address : Urban/Rural

• Religion : Hindu / Muslim/Christian/Others

• Family Type : Nuclear/Joint

• Number of children : Living alone/with children.

B – ILLNESS DETAILS

• Diagnosis

• Duration of illness

Duration of treatment

• Mode of treatment – Immunosupressants/ Steroids.

Current dose of steroids

Highest dose of steroids

• Complication of disease (if any)

• Other details (if any)

• Drug compliance (Good, poor)

• Perception of illness:

Extent of knowledge about illness.

• Previous treatment– Y/N.

• Psychological reaction: Fear/anger/grief/acceptance/denial

C- PAST HISTORY

• Mental illness – Y/N

• Medical illness – Y/N

• Past H/o of treatment for present complaints – other Modalities (specify)

• Suicidal attempt / gestures

• Drug intake → OC/Native treatment / HRT / Others

D- FAMILY HISTORY

• Type of family – Nuclear /Joint

• Family H/o of mental illness / Suicide / Alcohol abuse / Similar illness.

E-PERSONAL HISTORY

• Birth & Development history

• Menarche – age Menopause:

• Married Y/N

• Children Y/N

• Smoker Y/N

• Alcoholic Y/N

• Ganja Y/N

• Other substance use / abuse/dependence

• Sexual dysfunction – absent / present

(Frequency reduced / abstinent)

F- PREMORBID PERSONALITY

G – MENTAL STATUS EXAM

• Conscious : Y/N

• Rapport : Good/Possible/Not Possible

• Gaze Contact : Maintained / Possible/ Not possible

• Dressing and grooming: Adequate/Average/Poor

• Psychomotor activity : Increased/Normal/Decreased

• Attention : Aroused/Not aroused

• Concentration : Sustained/ Not sustained

• Memory : Immediate Y/N / Recent Y/N / Remote Y/N

• Orientation : Time Y/N / Place: Y/N / Person: Y/N

TALK

• Quantum : Decreased /Normal/Increased

• Tone : Decreased/Normal/Increased

• Tempo : Decreased/Normal/Increased

• Reaction time : decreased/Normal/Increased

• Prosody : Maintained/Not maintained

• Relevant : Y/N

• Coherent : Y/N

THOUGHT

• Formal thought disorder Y/N (Please specify)

• Delusions : Y/N (Please Specify)

• Hallucination : Y/N (Please Specify)

• Depressive ideas : Y/N

• Suicidal ideation : Y/N

MOOD

INSIGHT

Absent / Partial /Present

PHYSICAL EXAMINATION

NEUROLOGICAL EXAMINATION

APPENDIX II

HAMILTON DEPRESSION RATING SCALE (HAM-D)

SL.NO	ITEMS	0	1	2	3	4
1	Depressed Mood					
2	Feeling Of Guilt					
3	Suicide					
4	Insomnia[Early]					
5	Insomnia [Middle]					
6	Insomnia [Late]					
7	Work And Activities					-
8	Retardation					
9	Agitation					
10	Anxiety [Psychic]					
11	Anxiety [Somatic]					
12	Somatic Symptoms-Gastrointestinal					
13	Somatic Symptoms- General					
14	Genital Symptoms					
15	Hypochondriasis					-
16	Loss Of Weight					-
17	Insight					
18	Diurnal Variation					
19	Depersonalisation And Derealisation					
20	Paranoid Symptoms					
21	Obsessional And Compulsive Symptoms					

APPENDIX III

HAMILTON ANXIETY SCALE (HAM-A)

SL NO	ITEMS	0	1	2	3	4
1	Anxious Mood					
2	Tension					
3	Fears					
4	Insomnia					
5	Intellectual					
6	Depressed Mood					
7	Somatic Compliants : Muscular					
8	Somatic Compliants : Sensory					
9	Cardiovascular					
10	Respiratory					
11	Gastrointestinal					
12	Genitourinary					
13	Autonomic					
14	Behaviour At Interview					

APPENDIX IV

HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS)

	ITEMS	**3**	**2**	**1**	**0**
A	I feel tense or wound up				
A	Frightened feel of some awful happening				
A	Worrying thoughts				
A	I can sit at ease & relax				
A	Feeling of butterflies in stomach				
A	Feel restless				
A	Feelings of panic				

	ITEMS	**0**	**1**	**2**	**3**
D	Still enjoy things				
D	Can laugh				
D	Feel cheerful				
D	Slowed down				
D	Lost interest in appearance				
D	Look forward to enjoy things				
D	Entertainment				

APPENDIX V

BRIEF PSYCHIATRIC RATING SCALE (BPRS)

SL NO	ITEMS	0	1	2	3	4	5	6	7
1	Somatic concern								
2	Anxiety								
3	Emotional withdrawal								
4	Conceptual disorganisation								
5	Guilt feelings								
6	Tension								
7	Mannerisms & posturing								
8	Grandiosity								
9	Depressive mood								
10	Hostility								
11	Suspiciousness								
12	Hallucinatory behavior								
13	Motor retardation								
14	Uncooperativeness								
15	Unusual thought content								
16	Blunted affect								
17	Excitement								
18	Disorientation								

APPENDIX VI

MINI MENTAL STATE EXAMINATION

SL NO	ITEMS	SCORE
1	TIME Orientation	5
2	Place orientation	5
3	Registration of 3 words	3
4	Attention & calculation	5
5	Recall of 3 words	3
6	Naming	2
7	Repetition	1
8	Comprehension	3
9	Reading	1
10	Writing	1
11	Drawing	1

APPENDIX VII

CLOCK DRAWING TEST

Score	Error(s)	Examples
1	"Perfect"	No errors in the task
2	Minor visuospatial errors	a) Mildly impaired spacing of times b) Draws times outside circle c) Turns page while writing so that some numbers appear upside down d) Draws in lines (spokes) to orient spacing
3	Inaccurate representation of 10 after 11 when visuospatial organization is perfect or shows only minor deviations	a) Minute hand points to 10 b) Writes "10 after 11" c) Unable to make any denotation of time
4	Moderate visuospatial disorganization of times such that accurate denotation of 10 after 11 is impossible	a) Moderately poor spacing b) Omits numbers c) Perseveration: repeats circle or continues on past 12 to 13, 14, 15, etc. d) Right-left reversal: numbers drawn counter clockwise e) Dysgraphia: unable to write numbers accurately
5	Severe level of disorganization as described in scoring of 4	See examples for scoring of 4
6	No reasonable representation of a clock	a) No attempt at all b) No semblance of a clock at all c) Writes a word or name

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Archana G.
PG in MD Psychiatry
Madras Medical College ,Chennai -3

Dear Dr. Archana G.

The institutional ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled " Study of psychiatric manifestations and quality of life among patients with systemic lupus erythematosus" No. 04082012.

The following members of Ethics Committee were present in the meeting held on 24.08.2012 conducted at Madras Medical College, Chennai -3.

1.	Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2.	Prof. Pregna B. Dolia MD Vice Prinicpal, Madras Medical College, Chennai-3 Director , Inst. of Biochemistry, MMC, Ch-3	-- Member Secretary
3.	Prof. Kalaiselvi MD Prof of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Inst. of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. MD Ali M.D,. D.M., Prof & HOD, Dept. of MGE, MMC, Ch-3	-- Member
6.	Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
7.	Thiru. S. Govindsamy. BABL	-- Lawyer
8.	Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

ஆராய்ச்சி தகவல் தாள்

ஆய்வாளர் :

பங்கேற்பாளர் பெயர் :

தலைப்பு :

ஆராய்ச்சியின் நோக்கம் :

தாங்கள் இந்த மருத்துவ ஆய்வில் கலந்து கொள்ளுமாறு அழைக்கிறோம். இந்த ஆய்வானது எந்தவொரு மருத்துவ தலையீடும் இல்லாதது.

இதில் உங்களுக்கு எந்தவொரு ஆதாயமோ அல்லது ஆபத்தோ இருக்காது.

எங்கள் மையத்தில் நடைபெற இருக்கும் ஓர் ஆராய்ச்சிக்கு உங்கள் ஒத்துழைப்பும், ஒப்புதலையும் வேண்டுகிறோம்.

முடிவுகளை அல்லது கருத்தகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆய்வின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.


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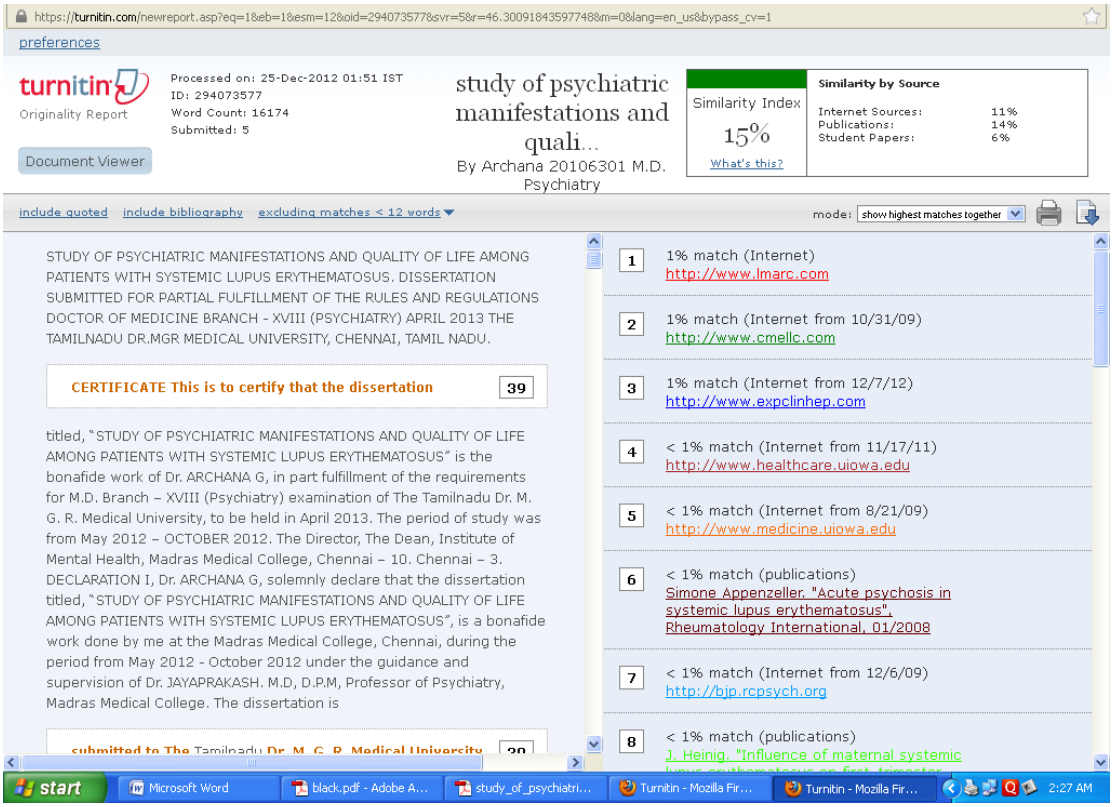
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